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Synthetic Applications of Heteroaromatic Betaines with Six-Membered Rings[1]

New synthetic methods (14)

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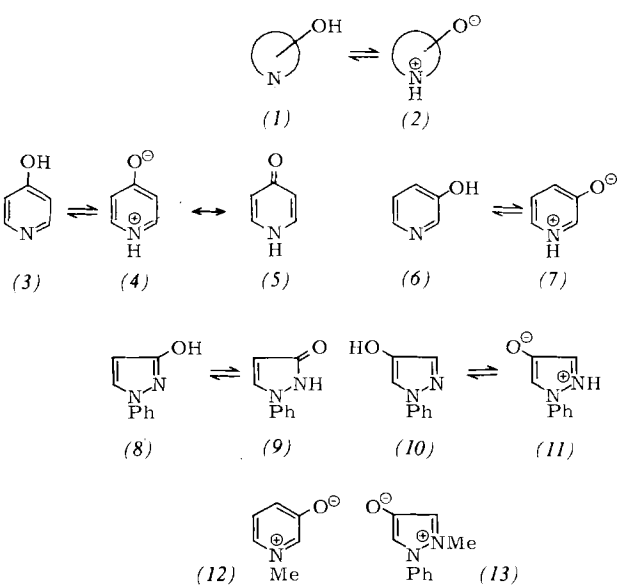
The cycloadditions of 3-hydroxy-1-methylpyridinium betaines with electron-deficient olefins have been extended to a variety of 1-substituents in place of methyl. Application of resonance theory and later of quantum chemical methods led to rationalization of preceding results and prediction of new reactions. Thermal additions of 2π- and 6π-electron addends at the 2,6-positions and of 4π-electron addends at the 2,4-positions are described. The cycloadducts are highly interesting potential synthetic building blocks.

1. Introduction[***]

Our interest in heteroaromatic betaines was initially aroused by our work on the tautomerism of heterocycles[2]. Heterocycles containing a ring nitrogen atom and a substituent hydroxyl group *(1)* are in tautomeric equilibrium with species *(2)* in which the proton has been transferred to the nitrogen atom. In *(2)* this is written in a zwitterionic form; in many cases, *e.g.* 4-pyridinol *(3)*, the zwitterionic form *(4)* is a resonance structure of a carbonyl compound, as 4-pyridone *(5)*. However when the hydroxyl group is situated β to the nitrogen, as in 3-pyridinol *(6)*, the alternative tautomeric form *(7)* has to be written in the betaine form. Similar possibilities exist in the five-membered ring series; thus, 3-hydroxypyrazoles *(8)* are tautomeric with 3-pyrazolones *(9)* while 4-hydroxypyrazoles *(10)* have zwitterionic tautomers *(11)*. If now the hydrogen attached to nitrogen in the tautomeric species *(7)* and *(11)* is replaced by a methyl group, we arrive at true heteroaromatic betaines *(12)* and *(13)*.



(1) (2) (3) (4) (5) (6) (7) (8) (9) (10) (11) (12) (13)

Heteroaromatic betaines with five-membered rings are known as mesoionic compounds and have been extensively investigated[3]. One of their most interesting properties is that they behave as 1,3 dipoles and undergo 1,3 dipolar additions with a great variety of dipolarophiles[4]. Very much less work has been carried out on heteroaromatic betaines

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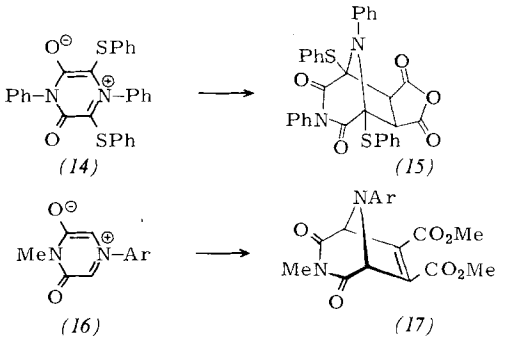
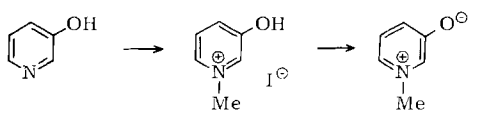
[***] The following abbreviations are used: Me = methyl, Et = ethyl, Ph = phenyl.

with six-membered ring systems of type *(12)*. At about the time we started our work, two short papers appeared giving examples of 1,3 dipolar cycloadditions involving heteroaromatic betaines having six-membered rings. *Honzl* and *Šorm*[5] found that the pyrazinium betaine *(14)* reacted with maleic anhydride to give *(15)*, and *Huisgen* and *Mäder*[6] described a rather similar reaction involving betaine *(16)* and dimethyl acetylenedicarboxylate to afford *(17)* in 70% yield.



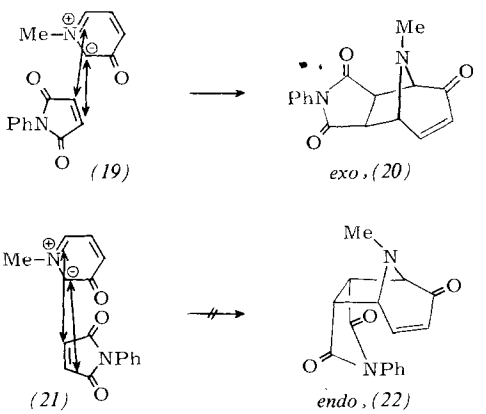
(14) *(15)* *(16)* *(17)*

We had at that time already started to investigate the simpler pyridinium systems and were able to prepare betaine *(12)* from 3-pyridinol *via* the quaternary salt *(18)*, which is most conveniently converted into *(12)* using an ion exchange



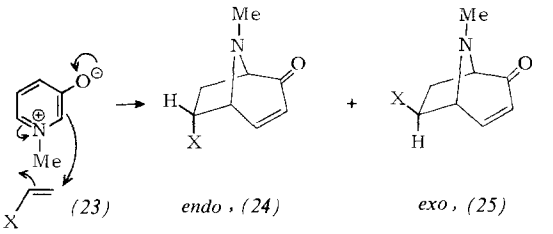
(6) *(18)* *(12)*

resin[7]. 1-Methyl-3-pyridiniumolate *(12)* is not a very pleasant compound with which to work. It is highly hygroscopic and difficult to crystallize. However it does show 1,3 dipolar activity[8] and with *N*-phenylmaleimide it reacts in the sense of *(19)* to yield the *exo*-isomer *(20)* rather than in the sense of *(21)* to give *(22)*.



(19) *exo*, *(20)* *(21)* *endo*, *(22)*

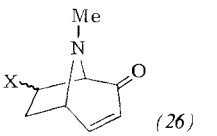
1-Methyl-3-pyridiniumolate *(12)* also reacts with acrylonitrile, methyl acrylate, methyl vinyl ketone, and methyl methacrylate. With each of these unsymmetrical dipolarophiles there are four conceivable reaction products that could be formed. In each case the reaction proceeds in the sense of *(23)* usually to produce a mixture of *endo (24)* and *exo (25)* isomers (Scheme 1). The two alternative regioisomers *(26)* were not detected in any of these reactions. Reactions were successful only with olefinic dipolarophiles containing a strongly electron-withdrawing group. Other olefins do not yield adducts.



(23) *endo*, *(24)* *exo*, *(25)*

Scheme 1. Cycloaddition of 1-methyl-3-pyridiniumolate; X = CN, CO_2CH_3; methyl methacrylate and *N*-phenylmaleimide also react.

The stereo and regio structures of the adducts were deduced from the ^{1}H-NMR spectra; for example, the *exo* adduct *(27)* from 1-methyl-3-pyridiniumolate and acrylonitrile gave the



(26)

NMR spectrum shown in Figure 1. The H-3 doublet is coupled with H-4, the H-4 quartet with H-3 and H-5. However H-5 is seen only as a doublet indicating coupling solely to H-4. The Karplus rule[9] and examination of models show that the coupling constant between H-5 and H-6-*endo* is expected to be very small, while that between H-5 and H-6-*exo* should be large. This at once locates the cyano group in the 6-*exo* position, and the rest of the spectrum confirms this assignment.

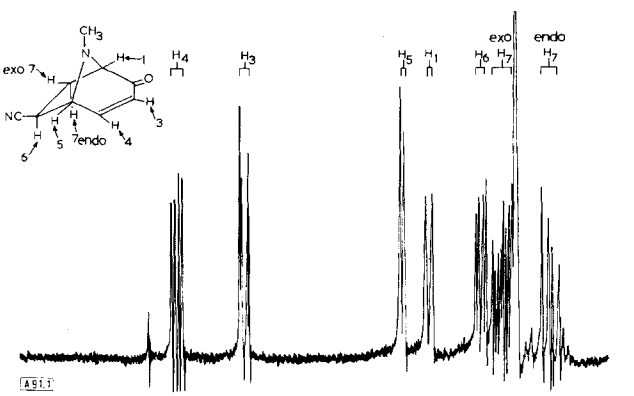


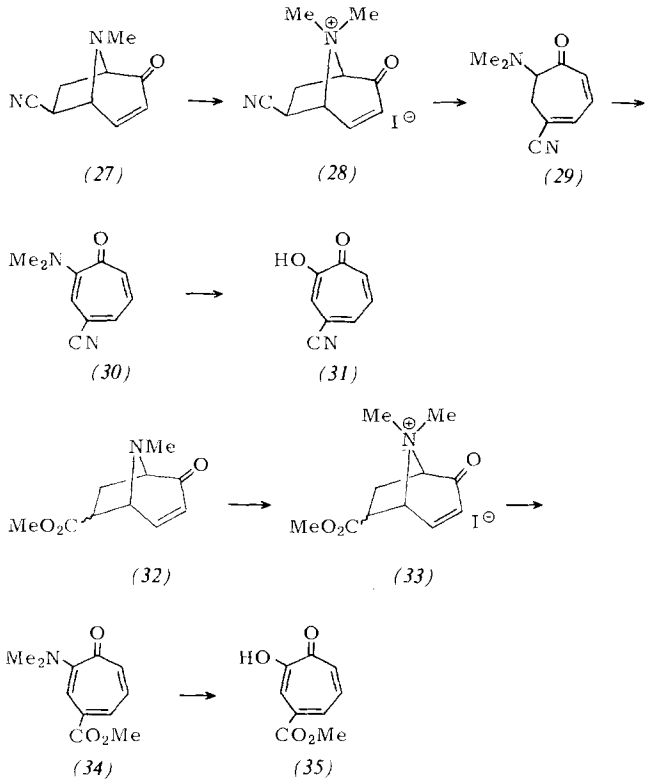
Fig. 1. ^{1}H-NMR spectrum of cycloadduct *exo*-8-methyl-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-carbonitrile *(27)* in $CDCl_3$.

2. Synthesis of Tropones

2.1. General

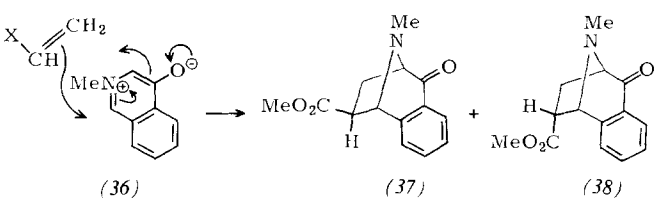
The structure of adduct *(27)* is reminiscent of the tropane alkaloids having the same ring system. One of the classical tropone syntheses is by Hofmann elimination[10] of the tropanes. We converted *(27)* to the methiodide *(28)*, which on reaction with silver oxide or sodium hydrogen carbonate gives the dimethylaminotropone *(30)*. Evidently the intermediate *(29)* undergoes dehydrogenation very easily; this is perhaps caused by oxygen in the air, but even with exclusion of oxygen we were unable to isolate *(29)* and therefore believe that it may disproportionate. The tropone *(30)* is easily hydrolyzed to the corresponding tropolone *(31)*. In this synthesis[11] of tropones and tropolones it is not necessary to separate the two stereoisomeric adducts; thus the mixture of adducts from methyl acrylate *(32)* is converted into the mixed methio-

dides *(33)* from which the tropone *(34)* and the tropolone *(35)* are then obtained (Scheme 2).

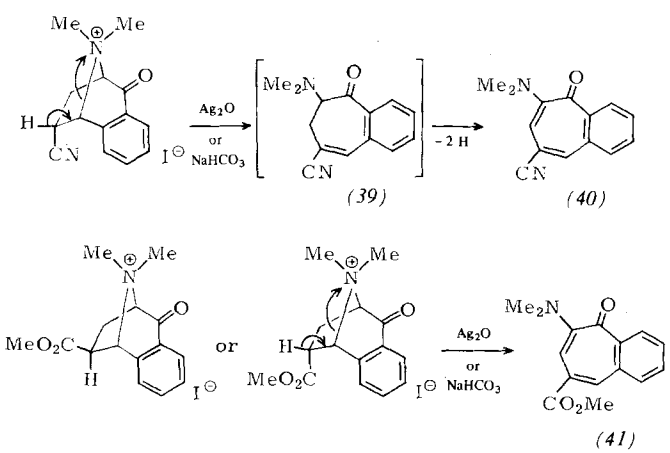


Scheme 2. Formation of tropolones.

This synthesis of tropones can be extended to benzotropones. The isoquinolinium betaine *(36)*[12] reacts as shown with dipolarophiles to again yield mixtures of isomeric adducts; thus, from methyl acrylate *(37)* and *(38)* were isolated (Scheme 3) and again the structures are shown clearly by the NMR spectra. The benzo-annelated tropones *(40)* and *(41)* were prepared from adducts of this type. Once



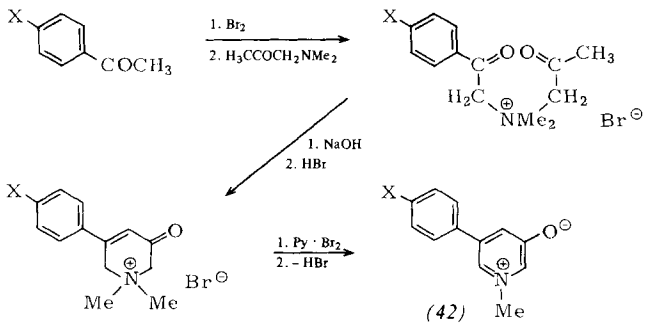
Scheme 3. 1,3-Dipolar additions of isoquinolinium betaine *(36)*. With methyl acrylate ($X=CO_2CH_3$) the isomers *(37)* and *(38)* are obtained.



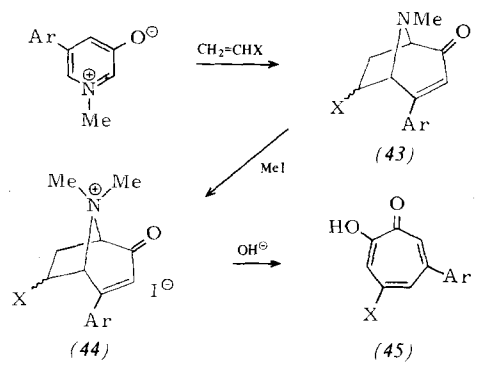
Scheme 4. Preparation of benzo-annelated tropones *(40)* and *(41)*.

again the postulated dihydro derivatives *(39)* could not be isolated (Scheme 4).

The synthesis can be extended to further substituted tropones. For example in Scheme 5 we give the preparation of 5-aryl-1-methyl-3-pyridiniumolates *(42)*[13]; these compounds readily form adducts *(43)*, which can be converted into quaternary salts *(44)* and thus into tropolones *(45)* (Scheme 6).

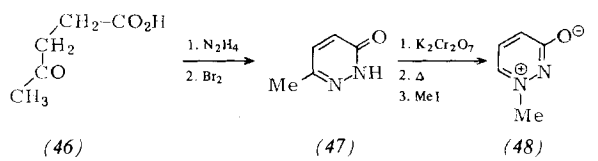


Scheme 5. Preparation of 5-aryl-1-methyl-3-pyridiniumolate *(42)*; X=H, OCH_3, NO_2.

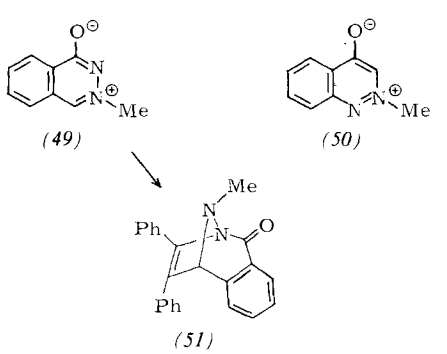


Scheme 6. Preparation of 6-aryl substituted tropolones *(45)*; X=CN, CO_2CH_3; Ar=C_6H_5, *p*-O_2N—C_6H_4, *p*-H_3CO—C_6H_4.

However the placement of further nitrogen atoms in the ring appears to seriously decrease the reactivity. Thus the methylpyridazinium betaine *(48)*[14] prepared as shown (Scheme 7) from *(46)* *via* *(47)* is unreactive toward a wide



Scheme 7. Preparation of 1-methyl-3-pyridaziniumolate *(48)*.



range of dipolarophiles, although the benzo analogs, *i.e.* the phthalazinium betaine[15] *(49)* and the cinnolinium betaine[14, 16, 17] *(50)* do show limited reactivity as 1,3 dipoles.

For example, reaction of *(49)* with diphenylacetylene gives the adduct *(51)*; the earliest example of such a cycloaddition, with the cinnolinium betaine *(50)*, was reported by *Lunt* and *Threlfall*[16].

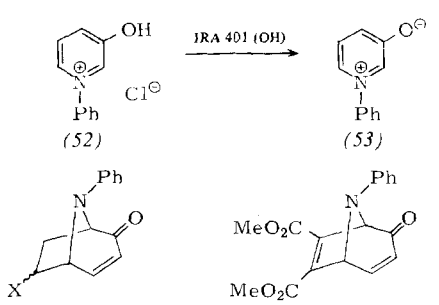
2.2. Synthetic Possibilities

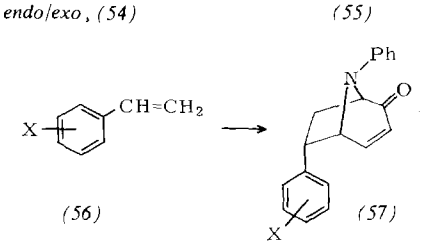
At this stage we might take stock of the synthetic potential of the above described route to tropones. It has indeed several advantages; utilization of readily available starting materials, formation of biologically interesting intermediates, and potential feasibility for large scale preparation. However, it must also be recognized that there are several pronounced disadvantages to the route as presented. The 1-methyl betaines are hygroscopic and difficult to crystallize, the yields of cycloadducts are often only moderate (in the range 30—50%), and the procedure is a somewhat tricky one. Indeed several times we have received enquiries from industrial companies who have encountered difficulties when trying to repeat some of the steps involved. The procedure is reproducible but we do find that some experience is needed to get the best results. Further, the reaction as described succeeds only with dipolarophiles containing strongly electron-withdrawing substituents, and it fails with the simple azine betaines.

In order to try and overcome these limitations, while retaining the advantages, there appeared to be two major alterations possible in the betaine structure: either we could vary the substituent carrying a negative charge and instead of oxygen incorporate nitrogen, carbon or sulfur; alternatively we could replace the methyl group on the nitrogen by other substituents. We have carried out considerable work on both these lines but it is the second that has produced the most interesting results; these will be dealt with in the following.

2.3. 1-Phenyl Betaines

A report[18] dating from 1905 states that the 3-hydroxy-1-phenylpyridinium chloride *(52)* can be produced in good yield from aniline and furfural. We found that this is indeed so and that *(52)* can be converted into the 1-phenyl betaine *(53)* using an ion exchange resin[7]. This 1-phenyl betaine is considerably easier to handle than the 1-methyl betaine,

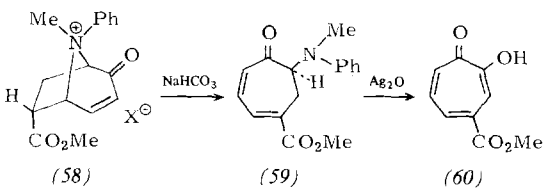




X = *p*-Cl, *p*-Br, 4-Pyridyl

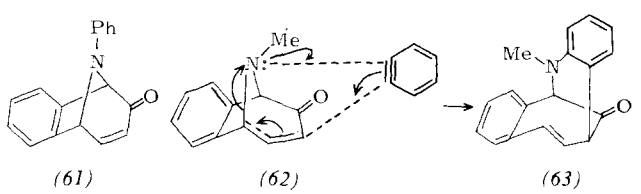
although it is still somewhat hygroscopic. Also it can be liberated *in situ*[19] from the hydrochloride and does react readily with a variety of dipolarophiles; thus mixtures of *endo* and *exo* products *(54)* can be produced[20] from *N*-phenylmaleimide, acrylonitrile, and methyl acrylate. Again only one set of regioisomers was found. Dimethyl acetylenedicarboxylate yielded *(55)* and the styrenes *(56)*[19] gave exclusively the *endo* adducts *(57)*, evidently because of steric reasons. The structures of all these adducts were again demonstrated from the ^{1}H-NMR spectra.

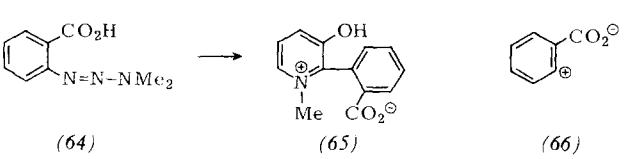
Conversion of the adducts of the 1-phenyl betaine into tropones is more difficult because of the low tendency of the adducts to form quaternary salts. However, using methyltrifluoromethanesulfonate[21], quaternary salts of type *(58)* could be prepared. With sodium hydrogen carbonate we were now able to isolate the dihydrotropone *(59)* which with silver oxide was converted smoothly to the tropolone *(60)* (Scheme 8). The stability of the intermediate dihydrotropone *(59)*—compared to the methyl analog—probably derives from steric effects.



Scheme 8. Preparation of the isolable dihydrotropone methyl-6-(methylphenylamino)-5-oxo-1,3-cycloheptadienecarboxylate *(59)* converted to the tropolone *(60)*.

Another difference between the 1-phenyl and 1-methyl betaines lies in their reactions with dehydrobenzene[22]. The 1-phenyl betaine yields[23] the expected adduct *(61)*; in the case of the 1-methyl betaine the corresponding adduct *(62)* is probably an intermediate—the isolated product[24] was *(63)*, the formation of which can be rationalized as shown by the cycloaddition of a further molecule of dehydrobenzene to *(62)*. Analogous[25–27] cases are known. In the reactions just mentioned, the dehydrobenzene was prepared[22] from

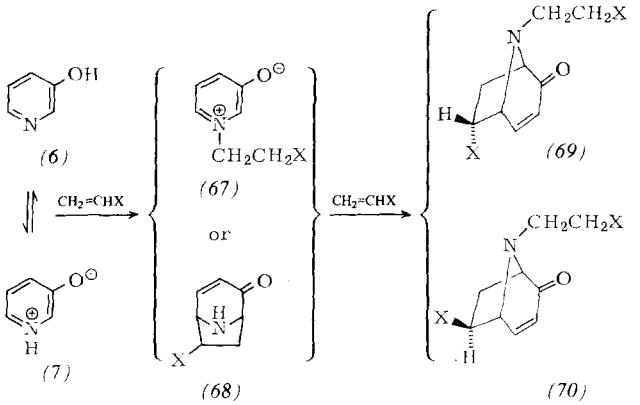




anthranilic acid and amyl nitrite. However, in an attempt to react the 1-methyl betaine with dehydrobenzene from the triazenobenzoic acid *(64)*[28] we obtained the product *(65)*, which could be formed by reaction of the 1-methyl betaine with the dehydrobenzene precursor *(66)*. There is ample previous evidence[29] for the intermediate formation of *(66)*.

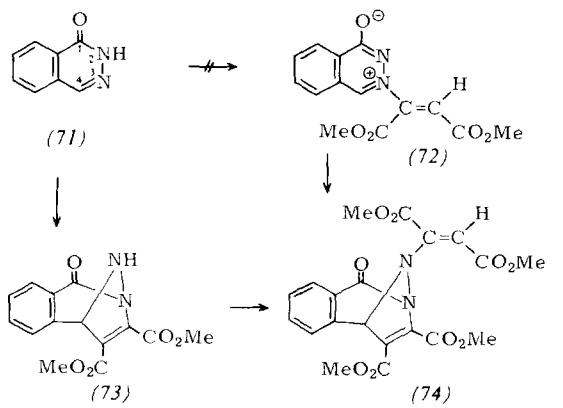
2.4. Betaines with Hydrogen as N-Substituent

As indicated in Section 1, 3-pyridinol *(6)* is a tautomeric compound in equilibrium with the zwitterionic form *(7)*. We now find that with acrylonitrile and methyl acrylate high yields of the *endo* and *exo* adducts *(69)* and *(70)* are formed (Scheme 9). Both adducts contain two molecules of the dipolarophile. Two reaction routes are possible: either initial reaction at the cyclic nitrogen atom with compounds of type *(67)* as intermediates, or alternatively dipolar addition with the betaine to give *(68)* followed by a Michael type addition at the nitrogen atom of *(68)*. Although no direct evidence is yet available to distinguish these possibilities in the reactions



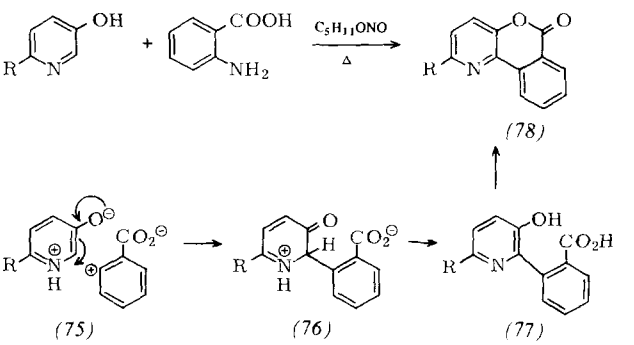
Scheme 9. Dipolar addition of 3-pyridinol *(6)* to acrylonitrile (X = CN), and methyl acrylate ($X = CO_2CH_3$).

of 3-pyridinols, there is, however, for the reaction of 1(2*H*)-phthalazinone *(71)*[30] with dimethyl acetylenedicarboxylate. The two possible routes are set out in Scheme 10; by following the NMR spectrum of the reaction we were able to show that adduct *(74)* was formed by way of intermediate *(73)* and not *(72)*. The signal at $\delta = 6.0$ is seen only at intermediate stages in the reaction; it is assigned to the bridgehead proton of the intermediate 1:1 cycloadduct *(73)*.



Scheme 10. Reaction of 1(2*H*)-phthalazinone *(71)* with dimethyl acetylenedicarboxylate.

The reactions of 3-pyridinols with dehydrobenzene are of interest. Under conditions where 3-pyridinols are allowed to react with excess diazotized anthranilic acid, the product is the expected adduct *(61)*, but when the 3-pyridinols are present in excess then the major product is the tricyclic compound *(78)*[31] formed *via* intermediates *(76)* and *(77)* by reaction of the dehydrobenzene precursor with the zwitterionic form [see *(75)*] (Scheme 11). This reaction is analogous to the formation of compound *(65)*.

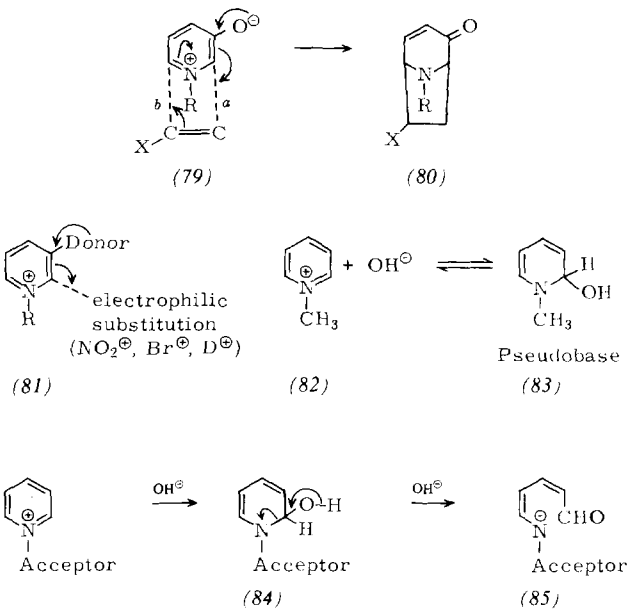


Scheme 11. Synthesis of [2]benzopyrano[4,3-*b*]pyridin-6-ones *(78)*; R = H or CH_3.

3. Mechanism of Cycloaddition

3.1. Valence Bond Treatment of the Cycloaddition Reactions

The regiospecificity of the cycloaddition *(79)* → *(80)* (R = methyl, phenyl, or hydrogen) together with the fact that group X of the dipolarophile needs to be an electron withdrawing substituent, can be explained. In the pyridinium compounds *(81)* the carbon atom at position 2 behaves as the most nucleophilic of the ring carbon atoms. Thus, electrophilic substitution of compounds of this type always occurs at C-2[32]; calculations show that this position has the highest π-electron density[33]. Evidently the bond *a* in *(79)*, between C-2 of the betaine and the C-β of the dipolarophile, is formed before bond *b*. A driving force in the reaction is the donation of electrons from the betaine to the dipolarophile (we believe, however, that these cycloaddition reactions are concerted and give evidence on this point in Section 3.3).



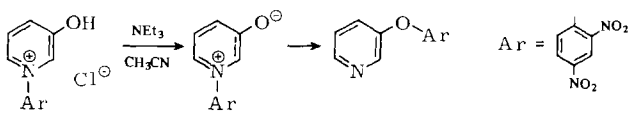
Scheme 12. Mechanism of 1,3-dipolar addition to betaine. Acceptor substituents are CN, SO_3, or 2,4-dinitrophenyl.

Obviously to extend the reaction to dipolarophiles with less electrophilic character, we need to increase the tendency to form bond *b*, and thus to reduce the electron density at the 6-position of the betaine. 1-Methyl- and 1-phenylpyridinium ions form pseudo bases [*e.g.* *(82)* → *(83)*] but this reaction is reversible and the proportion of pseudo base formed under normal conditions is very small[34]. The situation

changes dramatically when the substituent attached to nitrogen in the pyridinium ion is a strong electron accepting group, *e.g.* CN, SO_3, or 2,4-dinitrophenyl. In such cases the intermediate pseudo base *(84)* reacts further with hydroxide ion to give the open-ring product *(85)*[34] (Scheme 12). This reasoning led us to investigate betaines containing strongly electron accepting groups attached to the nitrogen atom.

3.2. 2,4-Dinitrophenyl Betaines

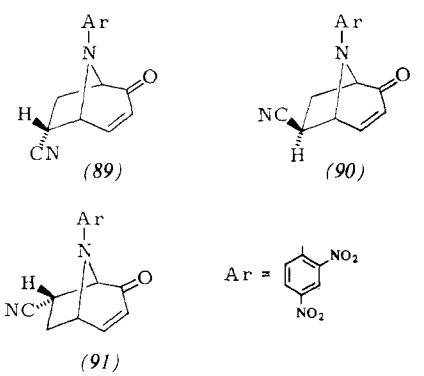
Vompe and *Turitsyna*[35] have reported that 3-pyridinol and 1-chloro-2,4-dinitrobenzene give the quaternary salt *(86)*, which, according to these authors, can be converted by sodium hydrogen carbonate into the betaine *(87)*. Actually, the product they obtained was the ether *(88)* (Scheme 13), which is quite unreactive towards dipolarophiles. We found that the betaine *(87)* can be isolated by treating the salt *(86)* with triethylamine in acetonitrile[36]. As expected it not only isomerizes readily to *(88)*, but also shows very pronounced



(86) *(87)* *(88)*

Scheme 13. Preparation of authentic 2,4-dinitrophenyl betaine 1-(2,4-dinitrophenyl)-3-pyridiniumolate *(87)*.

1,3-dipolar reactivity. Thus with acrylonitrile, in addition to the two expected adducts *(89)* and *(90)*, for the first time a third adduct was obtained in small yield: the regioisomer *(91)*.



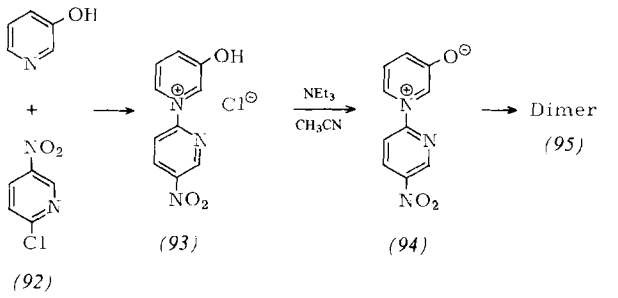
(89) *(90)*

(91)

Considerable further work with the dinitrophenyl betaines of the 3-pyridinols[36] and the 4-isoquinolinols[37] only revealed more clearly their tendency to rearrange to the ether. Because of this limitation we therefore turned to other *N*-substituents.

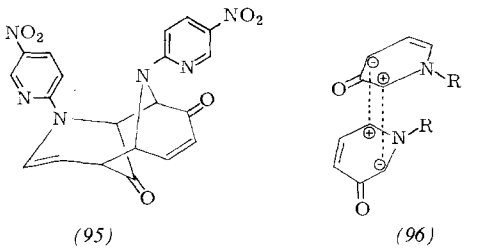
3.3. 5-Nitro-2-pyridyl Betaines

2-Chloro-5-nitropyridine *(92)* reacts readily with 3-pyridinol to give the quaternary salt *(93)* (Scheme 14). When the betaine *(94)* is liberated it soon spontaneously dimerizes to the compound *(95)*. This dimerization[38] involves the addition of the 2,6-positions of one betaine to the 2,4-positions of a second molecule in the sense of *(96)*. The complete stereo- and regiochemistry of the dimer is elucidated from the ^{1}H-NMR spectrum. Extensive decoupling experiments confirmed the assignments.



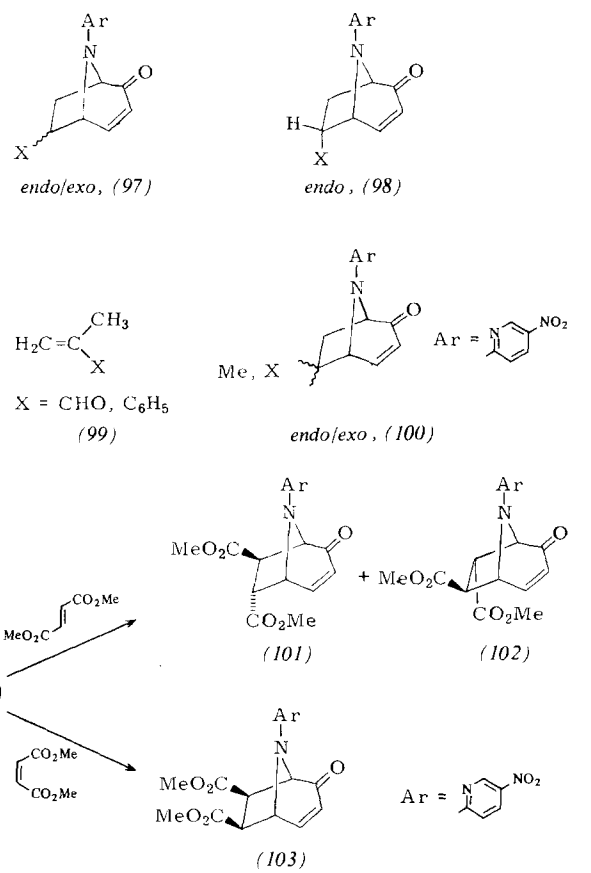
(92) *(93)* *(94)* *(95)*

Scheme 14. Dimerization of the betaine 1-(5-nitro-2-pyridyl)-3-pyridiniumolate *(94)* to *(95)*, m.p. = 169°C (dec.).



(95) *(96)*

Dimer *(95)* evidently dissociates reversibly at 100°C to the monomer, for under these conditions it reacts readily with a wide variety of dipolarophiles to give adducts[39] in good yields. Simple acrylic acid derivatives give mixtures of the *endo* and *exo* products *(97)*. Styrenes and similar compounds give only the *endo* compounds *(98)*, whereas 1,1-disubstituted dipolarophiles *(99)* give *endo* and *exo* compounds *(100)*. The reactions with dimethyl fumarate to give *(101)* and *(102)* and with dimethyl maleate to give *(103)* (Scheme 15) demonstrate the concerted character of the cycloadditions.



Scheme 15. Reactions of the betaine *(94)* with dimethyl fumarate and dimethyl maleate.

Thin layer chromatography showed the absence of the two adducts *(101)* and *(102)* in the reaction mixture from the dimethyl maleate addition, and conversely the absence of adduct *(103)* in the product from the dimethyl fumarate addition.

The nitropyridyl betaine dimer *(95)* also reacts with norbornene, diethyl azodicarboxylate, and various acetylenes. If the dimer fails to react, the monomer, which can be isolated under carefully controlled conditions from the quaternary salt *(93)*, sometimes gives a product. For example with ethyl vinyl ether the *endo* isomer *(98)*, X=OEt, is obtained.

3.4. Molecular Orbital Treatment of Cycloaddition Reactions

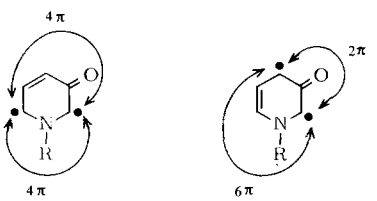
The valence bond rationalization given in Section 3.1 is unsatisfactory in several respects regarding the cycloadditions of the nitropyridyl betaine *(94)*. In particular it does not answer any of the following questions:

1. Why does the dimerization of the nitropyridyl betaine *(94)* involve the 2,6 positions of one molecule and the 2,4-positions of the other?

2. Why is the nitropyridyl betaine *(94)* so much more reactive than the dinitrophenyl betaine *(87)*?

3. Why does ethyl vinyl ether add in the same orientation as an electron deficient dipolarophile to the betaines?

The answer to the first of these questions is provided by application of the concept of orbital symmetry control to these additions. For additions at the 2,6-positions these betaines are 4π fragments; they can be considered as 5 atom fragments bridged by nitrogen or, alternatively, as 3 atom fragments bridged by a 3-carbon unit [cf. *(104)*]. They are thus expected to undergo suprafacial pericyclic reactions with 2π fragments—apart from dimerization all the reactions so far discussed come into this category.

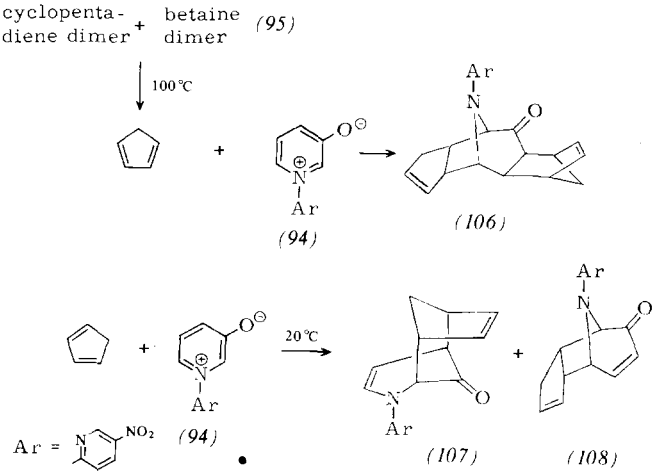


(104) *(105)*

For additions across the 2,4-positions [cf. *(105)*] the betaine can be considered either to be a 6π electron 5 atom fragment with a one carbon atom bridge, or as a 2π electron 3 atom fragment with a two-carbon and one-nitrogen atom bridge. In either case, suprafacial concerted thermal addition would be expected with a 4π fragment. This explains the dimerization and suggests, furthermore, that (a) other 4π fragments should add at the 2,4 positions, and (b) 6π fragments should add thermally at the 2,6-positions.

3.5. Reactions of Betaines with 4π Addends

The pyridyl betaine dimer *(95)* does indeed react with a variety of 1,3-dienes across the 2,4 positions[39]. In these reaction mixtures, the alternative possibility of the diene reacting as a mono-ene across the 2,6 positions also occurs. In suitable cases the reaction can be steered. Thus, if the reaction of *(95)* with cyclopentadiene is carried out at a high temperature—heating the two dimers together at 100 °C—the product

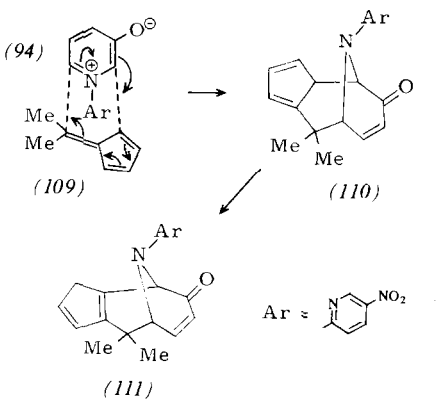


Scheme 16. Reactions of the dimeric pyridyl betaine *(95)* with dimeric cyclopentadiene at 100 °C giving adduct *(106)* (m.p. = 217 °C, 34%) and reaction of the corresponding monomer at 20 °C yielding the adducts *(107)* and *(108)* (m.p. = 194 °C (yield 45%) and 137 °C (yield 36%), resp.).

(106) is formed (Scheme 16). The initial step of the reaction is an addition of the diene as mono-ene across the 2,6 positions; this is followed by a Diels-Alder addition to give the final product. On the other hand, if the reaction between the two monomers is carried out at 20 °C, a mixture of the two expected initial products of addition across the 2,4 and 2,6 positions [*(107)* and *(108)*] is formed (Scheme 16).

3.6. Reaction of Betaines with 6π Addends

The nitropyridyl betaine *(94)* reacts with dimethylfulvene in the sense of *(109)*; the initial adduct *(110)* isomerizes spontaneously to the end product *(111)*. This is a general



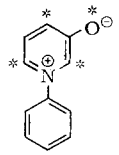
Scheme 17. Reaction of the pyridyl betaine *(94)* with dimethylfulvene.

reaction and similar products to *(111)* have been obtained from phenyl and *p*-methoxyphenylfulvene[39]. The structures of these adducts were again proved by the ^{1}H-NMR spectra.

3.7. Pyrimidinyl Betaines

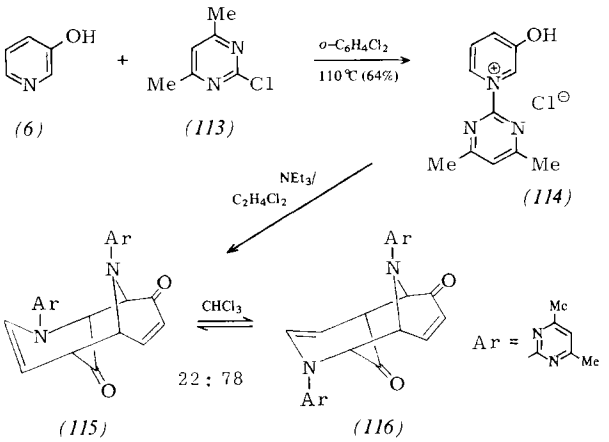
We now turn to the second question in Section 3.4. Why is the nitropyridyl betaine *(94)* more reactive than the dinitrophenyl betaine *(87)*? The reactivity can be measured in the tendency of the former to dimerize, whereas the latter does not. The tendency to dimerization should vary with the LUMO-HOMO energy difference. It is known that extended conjugation decreases this difference and hence we expect the dinitrophenyl betaine *(87)* to be more reactive than the

phenyl betaine *(53)* and this in turn to be more reactive than the methyl betaine *(12)*. This has in fact been confirmed experimentally. Aza substitution at the starred positions of the pyridine ring [see *(112)*] lower the HOMO and hence increase this difference. This explains why pyridazinium betaines such as *(14)* and *(16)* are much less reactive than pyridinium betaines.



(112)

Conversely, aza substitution at the non-starred positions of the pyridine ring and at all positions in the phenyl ring will lower the LUMO; this and the small degree of twisting about the N—C bond explains the high reactivity of the pyridyl betaine *(94)*. This line of argument would further predict that a 1-pyrimidinylpyridinium betaine should be even more reactive. We have recently tested this prediction and found it to be correct[39].



Scheme 18. Synthesis of the dimers *(115)* and *(116)*.

The chloropyrimidine *(113)* reacts with 3-pyridinol *(6)* to give the quaternary salt *(114)*. On treatment with triethylamine in dichloroethane this yields a mixture of two dimers, *(115)* and *(116)* (Scheme 18). Initially the mixture contains only *(115)*, but on standing for several hours the other dimer *(116)* predominates; the mixture at equilibrium contains 78% of *(116)*. The complete structures of the two dimers and their stereochemistry were deduced from the ^{1}H-NMR spectra using extensive decoupling.

In dimerizations of this type there are four possible regio- and stereoisomers (see Scheme 19). In $_\pi4_s+_\pi6_s$ processes[40], *exo* adducts are generally favored. The kinetically controlled products are the *exo* 2,2′-4,6′ derivatives: this isomer is formed exclusively in the dimerization of pyridyl betaine *(94)* to *(95)*, and as initial product in the case of pyrimidinyl betaine *(115)*.

Equation (1)[41] describes the energy for addition at positions rr′ of R to ss′ of S.

$$\Delta E = K\frac{[(C_r^{HO}C_s^{LU}+C_{r'}^{HO}C_{s'}^{LU})\gamma]^2}{E_R^{HO}-E_S^{LU}}+\frac{[(C_r^{LU}C_s^{HO}+C_{r'}^{LU}C_{s'}^{HO})\gamma]^2}{E_S^{HO}-E_R^{LU}} \quad (1)$$

Using the CNDO/2 method[33] we have calculated the HOMO and LUMO coefficients for 1-methylpyridinium betaine *(12)* (Fig. 2); these calculations do indeed predict initial formation of the *exo* 2,2′-4,6′ isomer. In the case of the pyridyl betaine dimer *(95)* the dimerization reaction is only weakly reversible at room temperature so this remains the major product. However, the pyrimidinyl betaine-dimer system, which is much more reactive and probably contains an appreciable amount of monomer in equilibrium, changes fairly rapidly until the dimer *(116)* predominates, which is probably favored on steric grounds over *(115)*.

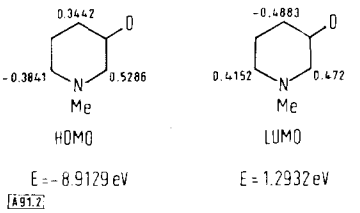
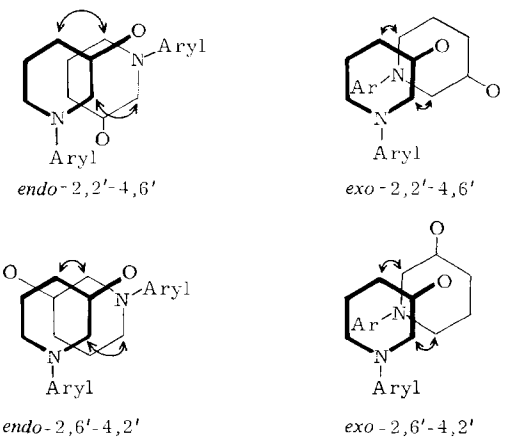


Fig. 2. HOMO and LUMO coefficients of 1-methyl-3-pyridiniumolate *(12)*. ΔE (in eV) is

$-3.51\times10^{-2}\gamma^{-2}$ for 2,2′–4,6′
and $-3.41\times10^{-2}\gamma^{-2}$ for 2,6′–4,2′



Scheme 19. Regio- and stereoselectivity of the dimerization of 1-aryl-3-pyridiniumolates.

Preliminary work with the pyrimidinyl betaine showed that it is exceedingly reactive with a wide variety of addends. We believe that the application of these reactions will be of considerable significance in the synthesis of hetero- and carbocyclic compounds with 7—10 membered rings.

3.8. FMO Control of Orientation of Addition of the 2π Electron System

The VB rationalization given in Section 3.1 (Scheme 12) for the exclusive formation of regioisomers of type *(24)* and *(25)* to the exclusion of *(26)*, clearly does not explain why the same orientation of addition is observed in the case of vinyl ethers as in the case of electron-deficient olefins. The third question posed in Section 3.4 has still to be answered. Comparison of the HOMO and LUMO values for 1-methyl-3-pyridiniumolate (Fig. 2) with the corresponding coefficients for (a) electron-deficient and (b) electron-rich olefins shows that the orientations *(24)* and *(25)* are preferred over *(26)* *in both cases*[38, 39], although in (a) the betaine HOMO/olefin LUMO interaction is dominant, while in (b) the betaine LUMO/olefin HOMO interaction is stronger.

Thanks are due to the many dedicated workers who have helped in this research: Badreldin Ibrahim, Taisuke Matsuo, Muthyala Ramaiah, Stuart K. Parton, Roberto Rittner, Ivan Taulov, Julie Barnerji, Judit Frank, Horst Wilde, Lemi Turker, Hussein Dowlatshahi, and Gabi Sabounji.

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Biomimetic Polyene Cyclizations

By William S. Johnson[*]

Certain polyenic substances having *trans* olefinic bonds in a 1,5 relationship can be induced to undergo stereospecific, non-enzymic, cationic cyclization to give polycyclic products with all-*trans* ("natural") configuration. These transformations appear to mimic in principle the biogenetic conversion of squalene into polycyclic triterpenoids. Acetal and allylic alcohol functions are effective initiators for these cyclizations, and methylacetylenic end groups are particularly useful terminators since they lead to five-membered rings. Thus a tetraenic acetal having no chiral centers has been converted in a single step into a tetracyclic product having seven such centers. The process is highly stereoselective, giving only two of 64 possible racemates. Systems have also been developed for effecting the total synthesis of the steroid nucleus in a single step starting from a substrate containing only one ring. The mechanism of these biomimetic cyclizations and also that of their enzymic counterparts is still unknown, but the balance of the evidence favors a synchronous process.

1. Introduction

The strategy for the total synthesis of polycyclic natural products, particularly the steroid and polycyclic triterpenoids, has involved, for the most part, step-by-step annelations, *i.e.*, each new ring is formed one at a time[1]. The biomimetic approach differs in that the plan envisages the production of a number of rings stereospecifically in a single step by the ring closure of an acyclic chain having appositely placed *trans* olefinic bonds, a process analogous to the known biogenetic conversion of squalene into polycyclic triterpenoids, *e.g.*, lanosterol[2], the precursor of cholesterol.

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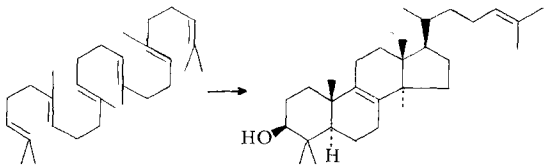
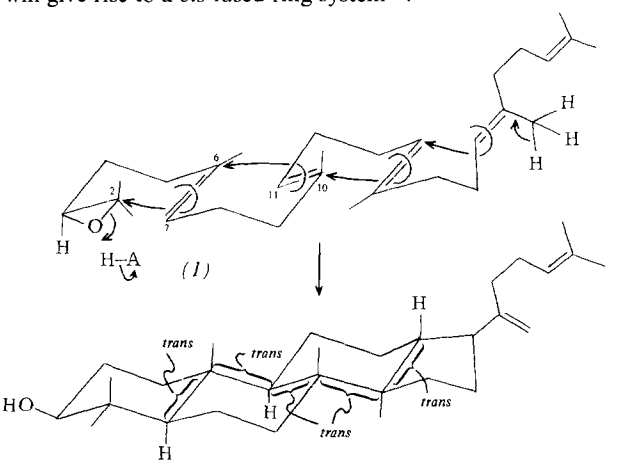


Squalene Lanosterol

In 1955 *Stork et al.*[3] and *Eschenmoser et al.*[4] pointed out that the stereochemical course of the biological cyclization of squalene could be rationalized on stereoelectronic grounds. Their important hypothesis, which immediately stimulated serious biomimetic studies, can be illustrated by considering the conversion of squalene oxide *(1)*, which is a known biogenetic intermediate[5], into the plant triterpenoid dammaradienol *(2)*. The process may be regarded as a sequence of *trans-anti-parallel* electrophilic additions to the olefinic bonds, in the same stereochemical sense that bromine adds stereospecifically to alkenes. Thus protonation of the oxygen atom of squalene oxide *(1)* generates an incipient cationic center at C-2, which attacks the 6,7-olefinic bond, thereby initiating formation of the σ bond between C-2 and C-7. Concomitantly, the cationic center developing at C-6 starts an electrophilic attack on the 10,11-olefinic bond generating the σ bond between C-6 and C-11, *etc.* The addition of C-2 and C-11 to the 6,7-olefinic bond occurs in the *trans* manner, yielding the *trans*-fused ring system found in the product *(2)*. Thus the all-*trans* geometry of the olefinic bonds in squalene results in *trans,trans,trans,trans,trans*-fusion of the four rings in product *(2)*. A corollary to the hypothesis is that a *cis* olefinic bond will give rise to a *cis*-fused ring system[6].



(2)

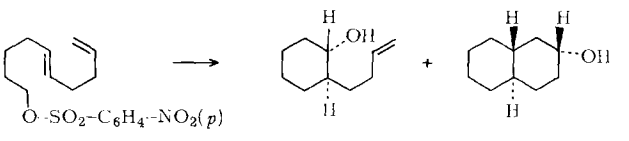
The first studies directed toward non-enzymic biogenetic-like polyene cyclization involved attempts to initiate cyclization by protonation of the terminal olefinic bond of a polyene chain[3, 7, 8]. The results were not promising[6]. Seemingly, much of the difficulty that has been encountered in the acid-catalyzed cyclization of such systems, including squalene, can be attributed to the rather indiscriminate protonation of the substrate, initiating a variety of other cyclizations in addition to the desired reaction. Moreover, the relatively strong acidic conditions generally employed are known to be conducive to deprotonation (hence the production of partially cyclized products) as well as to promoting reactions such as addition to and isomerization of the olefinic bonds.

It was with the hope of obviating these difficulties that we initiated, in 1960, a search for polyolefinic substrates containing an appropriately positioned functional group that could be used to generate a cyclizable cationic carbon center under conditions which would not otherwise affect the olefinic bonds. This requirement appears to be fulfilled, at least in part, by certain polyolefinic epoxides which have been examined extensively by *van Tamelen*[9]. Limitations in space preclude a review of these most interesting studies in the present paper. Other important studies that must be mentioned are the free radical- and mercuric ion-initiated cyclizations of *M. Julia*[10], and the proton- and mercuric ion-initiated cyclizations described by *Semenovsky*[11].

Our very first investigations on the solvolysis of polyenic sulfonate esters (see Section 2) gave useful mechanistic results; however, the yields of cyclized products were extremely poor. From an extensive search for groups more effective than sulfonate esters for initiating cationic polyene cyclizations, only two good initiators emerged: the acetal function and the allylic alcohol function. Our studies with these initiators are reviewed below.

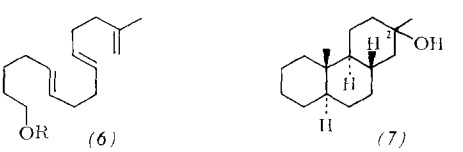
2. Cyclization-Solvolysis of Polyenyl Sulfonate Esters

Careful product analyses have been made of the mixtures obtained upon solvolysis of acyclic olefinic sulfonate esters designed to produce mono-[12], bi-[13], and tricyclic[14] systems[6]. Thus eleven products were identified from the formolysis of the 5,9-decadienyl *p*-nitrobenzenesulfonate *(3)*. The main component (after cleavage of the formate esters) was the monocyclic *trans* alcohol *(4)*, produced in 35% yield. The major bicyclic component was *trans,syn*-2-decalol *(5)* ("natural configuration"). Moreover, all of the bicyclic material (hydrocarbons as well as alcohols), which amounted to 12% yield, consisted exclusively of *trans*-decalin derivatives; no *cis* products were found[13a]. Formolysis of the geometric isomer of *(3)*, having a *cis* instead of a *trans* internal olefinic bond, gave a similar array of products except that they all belonged to the opposite stereochemical series. In particular, the bicyclic components, formed in 16% yield, all belonged to the *cis*-decalin series[13b]. Although the yields of bicyclic products were low, the stereospecificity of their formation represented the first example of a system that followed the theoretical predictions of *Stork*[3] and *Eschenmoser*[4] (see Section 1).



(3) (4) (5)

The product from the acetolysis of the trienyl sulfonate ester *(6)*, R=$SO_2C_6H_4$—NO_2(*p*), was estimated to consist of approximately 20% acyclic material [*(6)*, R=CH_3CO], 40% monocyclic, 8—12% bicyclic, and 2.8% tricyclic substances[14]. The tricyclic product, after cleavage of the acetates, was shown to be exclusively the *trans,trans,trans*-alcohol *(7)*

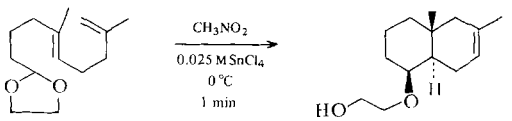


(6) (7)

as a mixture of C-2 epimers. Although the stereospecificity of the reaction was encouraging, the low yield was completely unacceptable.

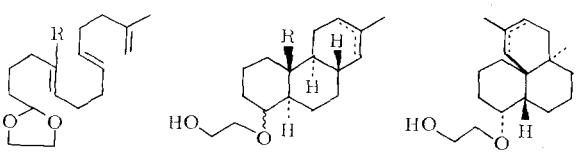
3. Cyclization of Polyenecarbaldehyde Acetals

After an exhaustive study of the cyclization of the *trans*-dienic acetal *(8)*[15, 6], conditions were found for its essentially quantitative conversion into *trans*-bicyclic materials, the major product being the substance *(9)*. It was also demonstrated that the isomeric form of *(8)* with the *cis* internal olefinic bond yielded only *cis*-decalin derivatives, in accordance with the theoretical predictions (see Section 1).



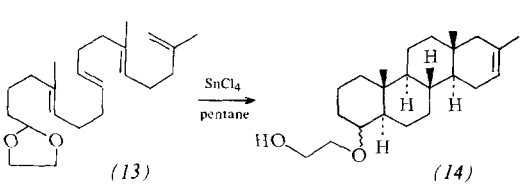
(8) *(9)*

The next objective was to examine the possibility of forming three rings from trienic acetals. Thus the *trans,trans*-acetal *(10)*, R = H, on treatment with stannic chloride in benzene, was converted into a mixture of tricyclic products *(11)*, R = H, all of which belonged to the *trans,trans,trans* ("natural") stereochemical series[14]. Similarly the acetal *(10)*, $R = CH_3$, was converted, in 63 % yield, into the mixture of all-*trans* tricyclic products *(11)*, $R = CH_3$[16]. Surprisingly, when the acetal *(10)*, $R = CH_3$, was cyclized with stannic chloride in nitromethane—conditions which had been so successful with the dienic acetal *(8)*—the reaction took a completely abnormal course involving rearrangement and yielded as the main product (44 % yield) the tricyclic substance *(12)*, whose constitution was established by single crystal X-ray diffraction analysis of a derivative[16].



(10) *(11)* *(12)*

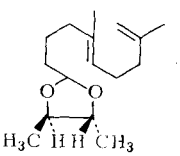
To determine if four rings could be produced in a single step, the cyclization of the tetraenic acetal *(13)* was examined[17]. This substance, on treatment with stannic chloride in pentane, was converted into a mixture of two crystalline D-homosteroidal tetracyclic epimers *(14)*, which belonged exclusively to the all-*trans* stereochemical series. This cyclization, which involves the production of no less than seven asymmetric centers and in this sense is comparable to the conversion of squalene into lanosterol, is remarkably stereoselective, yielding only two of 64 possible racemates. The constitution of *(14)* was established by degradation of the hydroxyethyl side-chain to give the 4-keto compound (the same product was formed from each epimer), and then interrelating



(13) *(14)*

the Wolff-Kishner reduction product with a substance synthesized from a naturally-derived D-homosteroid.

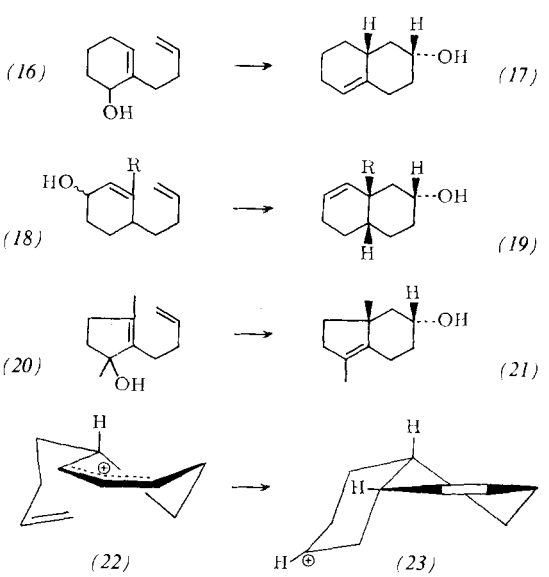
It is important to note that the products of all the biomimetic cyclizations described above were racemic. Thus the tetracyclic products represented by formula *(14)* contained an equal amount of the mirror image of *(14)*. The enzymic cyclization of squalene, on the other hand, proceeds with total asymmetric induction to produce only one enantiomeric form of the polycyclic products. In an effort to simulate this result in a non-enzymic process, we examined the case of the optically active dienic acetal *(15)* derived from (−)-butanediol (*R,R* configuration)[18]. Treatment of *(15)* with stannic chloride in benzene gave bicyclic products which were shown to have enantiomeric ratios of 92 : 8. Thus a very high degree of asymmetric induction has been realized. It will be interesting to see if this strong induction is found in the tetracyclic series.



(15)

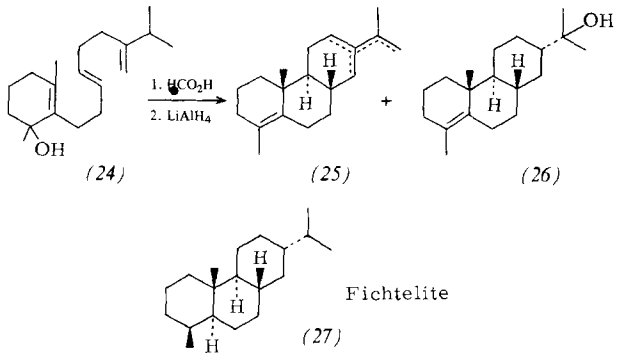
4. Cyclizations Promoted by the Allylic Cation

This type of cyclization is exemplified by the following conversions[6] which are catalyzed by formic acid: *(16)*→*(17)*[19], *(18)*→*(19)*[19, 20], and *(20)*→*(21)*[24a]. The stereospecific formation of the *cis*-fused ring system *(19)* from *(18)* is the expected consequence of the known preference for a cyclohexenyl cation to react with a nucleophile so as to form a *pseudo*-axial bond [see *(22)*→*(23)*].

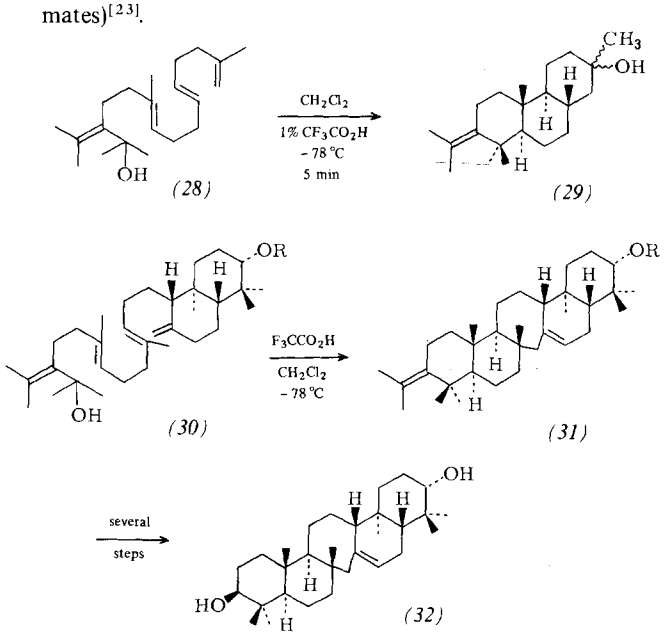


(16) *(17)* *(18)* *(19)* *(20)* *(21)* *(22)* *(23)*

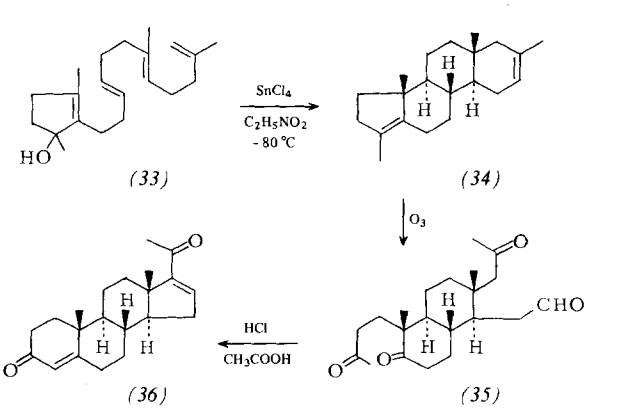
The formation of two new rings by allylic cation promoted cyclization is an efficient process. Thus the trienol *(24)* was quantitatively converted, by the action of cold formic acid, into a mixture of tricyclic products *(25)* and *(26)*. The reaction was stereospecific with respect to the ring fusion *(trans,trans)* as shown by separation and acid-catalyzed interconversion of each of the products, and by their reductive transformation into the natural product (±)-fichtelite *(27)*[21, 6].



Examples of the formation of three new rings follow. The tetramethyl allylic alcohol function, as incorporated in the substrate *(28)*, is an effective cyclization initiator[22], and tricyclic material *(29)* is formed rapidly under exceedingly mild conditions (52% yield). An example of the use of this initiator to effect the total synthesis of a natural product is the cyclization of the tetraenol *(30)*, $R=Si(CH_3)_2t\text{-}C_4H_9$, which involves the formation of three new rings including a seven-membered C-ring. The main product *(31)*, $R=Si(CH_3)_2t\text{-}C_4H_9$, could be converted, *via* selective oxidation of the isopropylidene group followed by reduction and deblocking, into (±)-serratenediol *(32)*, a pentacyclic triterpenoid with nine asymmetric centers (256 possible racemates)[23].

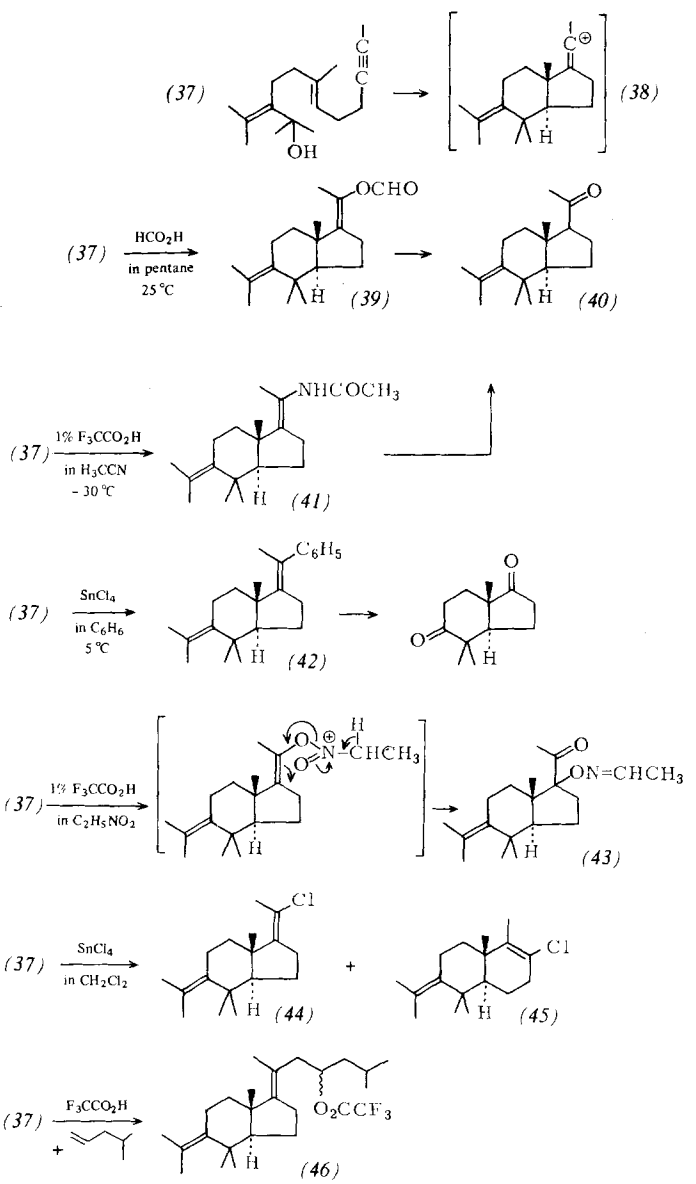


The total synthesis of a steroid was effected *via* cyclization of the tetraenol *(33)* which afforded (70% yield) the crystalline tetracyclic hydrocarbon *(34)*[24]. Ozonolysis of *(34)* gave (65% yield) the triketo aldehyde *(35)* which still retained the five new asymmetric centers that were generated in the cyclization step. Substance *(35)* was finally converted, through a double intramolecular aldol cyclodehydration, into (±)-16,17-dehydroprogesterone *(36)*.



5. Cyclizations Involving Participation of Acetylenic Bonds; Formation of Five-Membered Rings

Because the five-membered ring widely occurs in natural products, particularly in the D ring of steroids, it was of special interest to search for systems which would give five-membered ring closure in biomimetic processes. Since CC triple bonds located in the 5,6-position relative to a developing cationic center have a tendency to cyclize so as to give five-membered rings[25], it seemed reasonable to examine the behavior of such bonds as participants in polyene cyclizations. The dienynol *(37)* was examined as a model system and it did indeed undergo facile acid-catalyzed cyclization to give exclusively the 6/5 *trans*-fused ring system in high yield[26]. Thus upon treatment of *(37)* with formic acid, the enol formate

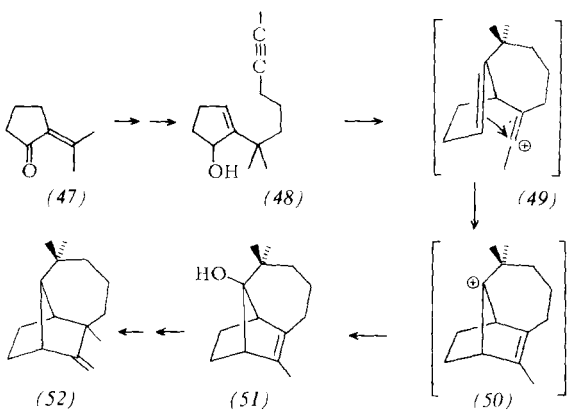


(39)[*] was produced in >90% yield. Hydrolysis yielded the ketone *(40)* which has all of the structural features of the C/D ring system of progesterone.

The cyclization of substance *(37)* involves either an intermediate or a transition state having the properties of a vinyl cation *(38)*. It is especially interesting that such cations can be generated efficiently under extremely mild conditions (*e.g.*, with 1% trifluoroacetic acid in a solvent at −78 °C) from a relatively stable ditertiary allylic cation. The energy for this transformation probably is provided by the conversion of π to σ bonds.

The vinyl cation *(38)* proved to be exceedingly reactive. Thus when it was generated in acetonitrile as the solvent, the nitrile reacted as a nucleophile giving, after work-up, the enamide *(41)*[*][26]. When stannic chloride in benzene—a system that had been employed successfully for the cyclization of olefinic acetals (see Section 3)—was used for the cyclization, the benzene was trapped by the vinyl cation giving the substance *(42)*[*][27]. Trifluoroacetic acid in nitroethane—which was the system of choice for the cyclization of the substrate *(33)* (see Section 4)—effected cyclization with capture of the nitroethane giving what proved to be the oxyimino compound *(43)*[28]. Another example of this type of cyclization is given below, *(53)*→*(68)*. Cyclization with stannic chloride in dichloromethane gave a mixture of five- and six-membered ring vinyl chlorides *(44)*[*] and *(45)*[29]. With trifluoroacetic acid in dichloromethane at −78 °C, the cyclization proceeded to give exclusively the six-membered ring chloride *(45)*, the "rearranged" vinyl cation evidently abstracting chloride ion from the solvent[30]. Finally it has been shown that the vinyl cation *(38)* can react with an alkene, *i.e.*, isohexene, to give the alkylation product *(46)*[*], thus developing the cholesterol-like side-chain. Vinyl cations can also react intramolecularly with olefinic bonds[26]. A case of special interest is described below.

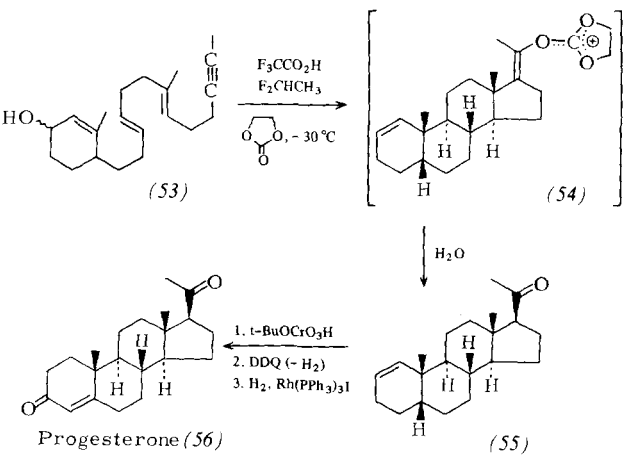
The cyclization of the cyclopentenol *(48)*, which is readily prepared in several steps *via* conjugate addition of the side-chain fragment to the unsaturated ketone *(47)*, proceeds, presumably *via* the cation *(49)* which reacts with the olefinic bond in the five-membered ring to form the 7-*anti*-norbornenyl type cation *(50)*. This tricyclic cation, on reaction with water added during work-up, is converted into the crystalline alcohol *(51)*. Under optimal conditions (CF_3CO_2H, 0 °C, 3 min) the yield for the conversion *(48)*→*(51)* is 75%. The structure of the alcohol *(51)* was established by its transformation



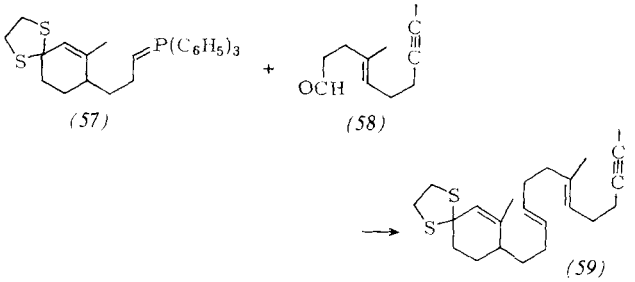
[*] The orientation of the substituents on the olefinic bond attached to the five-membered ring is unknown.

(several steps) into the natural product longifolene *(52)*, which was thus produced in 21% overall yield from 2-isopropylidenecyclopentanone *(47)*[31].

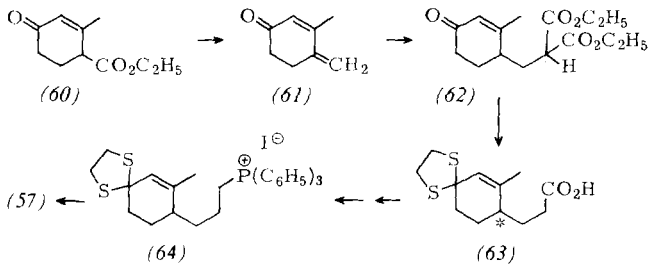
Attention is now turned to the total synthesis of steroids *via* the application of acetylenic participation in biomimetic polyene cyclizations. The trienynol *(53)* appeared to be a promising substrate for cyclization directly to the steroid nucleus. Indeed, under the indicated conditions, it was converted (65% yield) into the pregnenone *(55)* which, in turn, was readily transformed into progesterone *(56)*[32]. Ethylene carbonate was added to the cyclization mixture to serve as a nucleophile for capturing the vinyl cation, possibly in the form of the stabilized cation *(54)*.



Up to this point the synthesis of the cyclization substrates has been ignored. Attention is now turned to the preparation of the trienynol *(53)*[33]. A convergent approach was employed, the key step being the Wittig condensation of the phosphorane *(57)* with the aldehyde *(58)*. The Schlosser modification of the Wittig reaction was used in order to produce a *trans* olefinic bond in the product *(59)*. The conversion of substance *(59)* into the substrate *(53)* involved hydrolysis of the thio ketal to the unsaturated ketone which was reduced with lithium tetrahydridoaluminate.

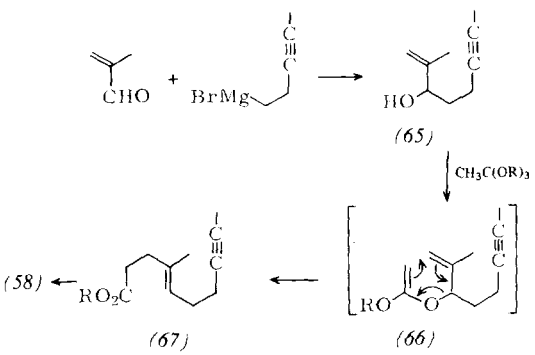


The phosphonium salt *(64)*, required for making the phosphorane *(57)*, was prepared from commercially available Hagemann's ester *(60)*. Conversion to the ethylene ketal followed by reduction with lithium tetrahydridoaluminate, then acid hydrolysis (which also effected dehydration) yielded the dienone *(61)*. This substance underwent a 1,6-Michael addition with malonic ester, giving the keto diester *(62)* which, on hydrolytic decarboxylation followed by reaction with ethanedithiol, was converted into the thio ketal acid *(63)*. This acid has an asymmetric center (indicated by the asterisk) and could be resolved into the (+) and (−) forms as the salts of optically active α-methylbenzylamine. Use of the (+)

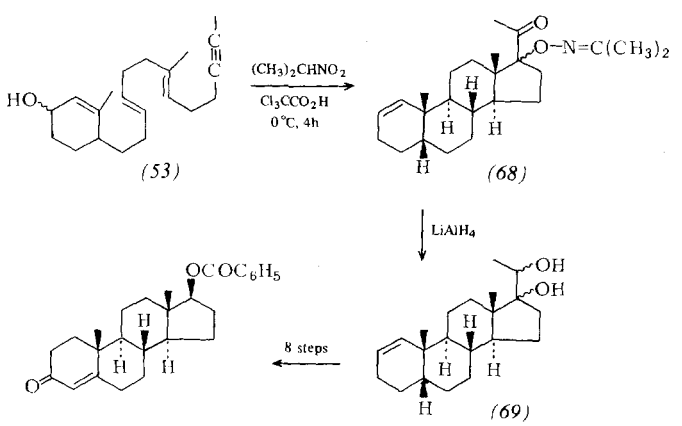


form of *(63)* in the remainder of the synthesis led to (+)-*(56)*, identical with natural progesterone.

The aldehyde *(58)* has been prepared in a variety of ways, one of which involves the addition of 3-pentynylmagnesium bromide to methacrolein. The resulting substituted allylic alcohol *(65)* was warmed with ethyl (or methyl) orthoacetate containing 5% propionic acid which effected the stereospecific orthoacetate Claisen reaction[34], involving the intermediacy of the ketene acetal *(66)*. The resulting enyne ester *(67)* was obtained in >90% yield, and the olefinic bond was >98% in the *trans* (*E*) form.

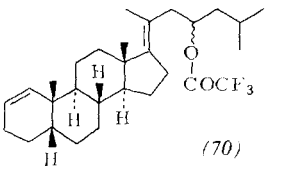


In other cyclization studies the trienynol *(53)* was treated with trichloroacetic acid in 2-nitropropane giving the oxyimino compound *(68)*[28], analogous to the formation of substance *(43)* (see above). This product was converted by hydrogenolysis with lithium tetrahydridoaluminate into the diol *(69)* which was transformed with periodate into the 17-keto compound and thence into testosterone benzoate[35].

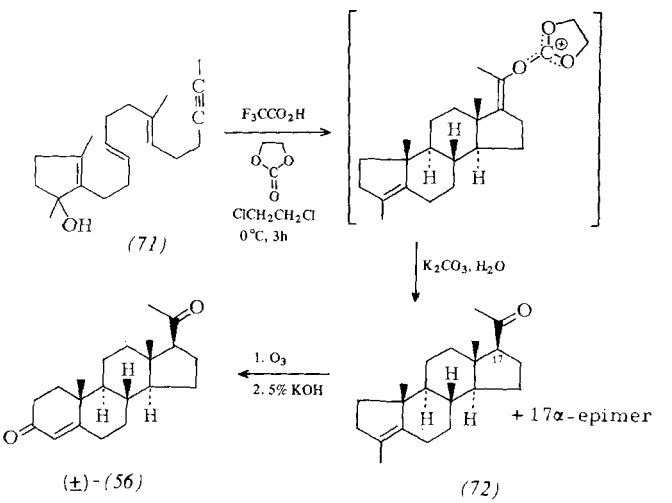


Testosterone benzoate

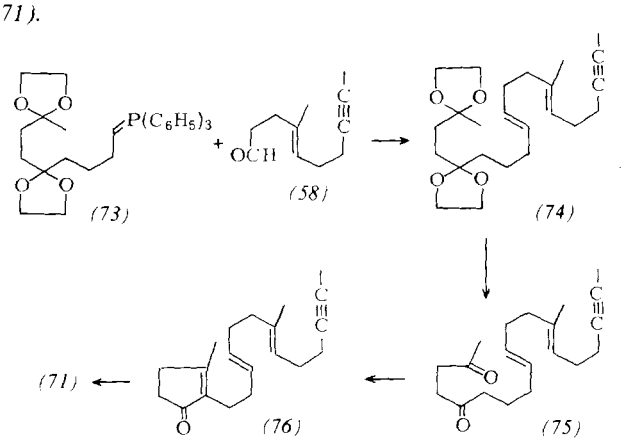
When the trienynol *(53)* was treated with trifluoroacetic acid in 1,1-difluoroethane containing isohexene at −60°C, the resulting vinyl cation reacted with the olefin (see above) to produce the adduct *(70)* in 30% yield[36]. The constitution of this product was proved by interrelationship with material produced from a natural steroid.



Another substrate that proved useful for synthesizing steroids is the cyclopentenol *(71)* which, on cyclization, produced the crystalline ketone *(72)* in 71% yield[26b]. Conversion of this product, *via* ozonolysis followed by intramolecular aldol condensation (see above), into (±)-progesterone was effected in >80% yield.



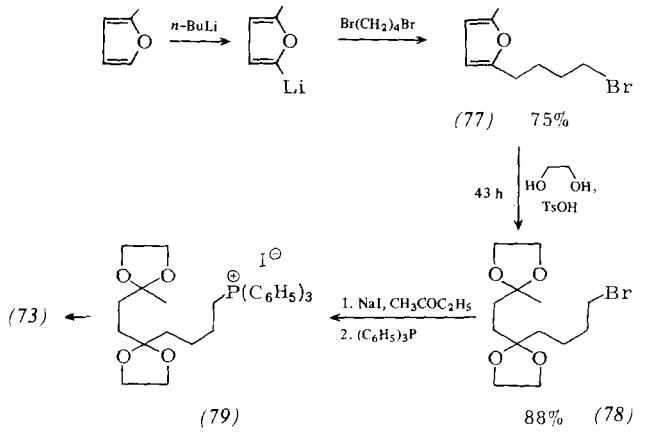
The synthesis of the cyclopentenol *(71)* was effected by the Wittig-Schlosser condensation of the aldehyde *(58)* (prepared as described above) with the phosphorane *(73)* as shown in the flow sheet. The product *(74)* was hydrolyzed to the diketone *(75)* which, in turn, was induced to undergo a base-catalyzed cyclodehydration, giving the unsaturated ketone *(76)*. Reaction of *(76)* with methyllithium gave the substrate *(71)*.



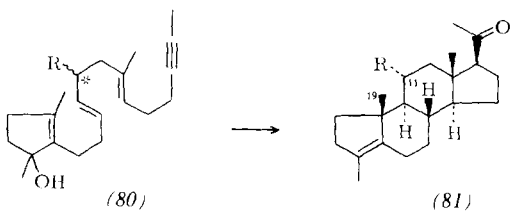
The synthesis of the phosphonium salt *(79)*, required for production of the aforementioned phosphorane *(73)*, was accomplished as summarized in the accompanying flow sheet. The step of particular interest is the cleavage of the furan ring of the alkylation product *(77)* under ketalization conditions, to give the diketal bromide *(78)*.

The cyclization of a number of substrates of the type shown by formula *(80)* has given only the 11α-substituted[*] products

[*] Steroid numbering.

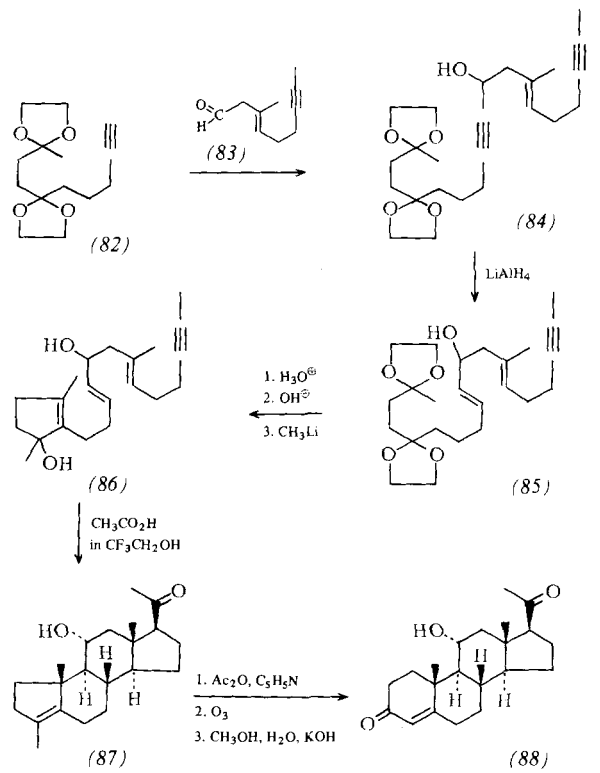


(81), probably because the transition state that would lead to the 11β-epimer involves serious non-bonded (1,3-diaxial type) interactions, *e.g.*, between the developing 11β-substituent and the C-19 methyl. Thus in the case where $R=CH_3$[37], $CH_2CCl=CH_2$[37], and $CH_2CH=CH_2$[37], the reaction *(80)*→*(81)*, which proceeded more slowly requiring more vigorous conditions than when R=H (see above), only one stereoisomeric form of the cyclized products *(87)* was produced in 50—60% yields. The exclusive formation of the 11α-epimer in the cyclization indicated that the reaction involves total asymmetric induction. Thus if the substrate *(80)* were obtained in one enantiomeric form with respect to the asymmetric carbon holding the R group, the product *(81)* should be optically pure. Preliminary studies of the cyclization of partially resolved substrate *(80)*, $R=CH_2CH=CH_2$, did indeed give an optically active tetracyclic product of undetermined enantiomeric purity[38].



In the cyclization *(86)*→*(87)*[39] the reaction appeared to be even slower than those mentioned above, requiring more severe conditions, perhaps because the nucleophilicity of the disubstituted olefinic bond was attenuated by the negative inductive effect of the allylic hydroxyl group. The best yield of the α-hydroxy tetracyclic product that has been produced to date is 40%[40]. Even so, a relatively efficient totally synthetic pathway to cortisone from simple chemicals has been defined[39] as follows:

The aldehyde *(83)* was prepared by reaction of the aforementioned allylic alcohol *(65)* with thionyl chloride to afford the allylically transposed chloride which, in turn, was condensed with the anion of dithiane. Hydrolysis of the product gave the aldehyde *(83)*. The diketal acetylene *(82)* was produced by reaction of lithium acetylide with the lower homolog of the diketal bromide *(78)*. Conversion of the tetracyclic product *(87)* into 11α-hydroxyprogesterone *(88)* was carried out *via* the oxidation-cyclodehydration sequence described above [*(72)*→*(56)*]. The substance *(88)* is a known intermediate in the commercial synthesis (*ca.* 50% overall yield) of hydrocortisone acetate. Although the yields have not been



optimized for a number of steps, the overall yield of *(88)* at the present stage of refinement is 15.4% in 16 steps from methacrolein and 2-methylfuran. The preparation and cyclization of the resolved form of the substrate *(86)* is under study.

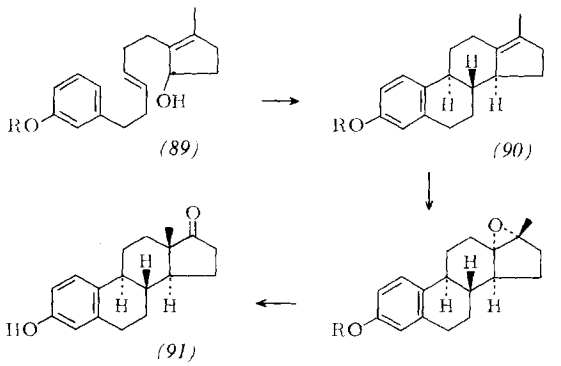
6. Concerning the Mechanism of Polyene Cyclizations

The question of the mechanism of stereospecific cationic polyene cyclizations, whether enzymic or biomimetic, has been open to debate. On the one hand, the intermediacy of partially cyclized cations (classical or bridged) has been shown to be consistent with the observed stereochemical course of such cyclizations[41]. On the other hand, a concerted process in which all of the new CC bonds are formed synchronously represents an equally satisfactory rationalization of the facts. There has been very little direct evidence obtained for deciding between the "stepwise" and the "synchronous" mechanisms; however, at the present time the balance (see below) is somewhat in favor of the latter.

It has been demonstrated by deuterium incorporation experiments that certain enzymic[42] as well as biomimetic[43] polyene cyclizations do not involve partially cyclized olefinic intermediates which would require reprotonation (and consequent deuterium incorporation) in order for the cyclization to continue. This finding, however, does not preclude a stepwise process involving cations which do not deprotonate.

Kinetic studies of solvolysis of a series of substituted dienic *p*-nitrobenzenesulfonates (see formula *(3)* above) in both acetic acid[44] and in trifluoroethanol[45] have shown small, but incremental, rate enhancements by substituting the vinyl hydrogens of the terminal olefinic bond by methyl groups. These effects represent a necessary, but not sufficient, condition for the synchronous mechanism. Other results consistent with the synchronous process are presented below.

In connection with a total synthesis of estrone *(91)* from *(89)*[46], a thorough study was made of the key step, namely



(89) (90) (91)

the Lewis acid-catalyzed biomimetic cyclization *(89)*→*(90)* which proceeds in high yield. In addition to the product *(90)*, there was always obtained some of the isomer resulting from cyclization *ortho*, instead of *para*, to the OR group. The *para*/*ortho* ratio varied depending on the nature of the allylic leaving group in the substrate[47]. For example, in the case of *(89)* having a free hydroxyl group, the ratio was 8.4; on the other hand, when the leaving group was trimethylsilyloxy the ratio was 2.6. Thus the effect of the leaving group is "felt" in the bonding of the aromatic nucleus to the internal olefinic bond, suggestive of a synchronous process. Moreover, kinetic studies of the cyclization of the substrate *(89)* having other groups (*i.e.*, CH_3, H, CF_3) in place of OH in the aromatic nucleus gave decreasing rates as the groups became more electronegative[47]. These findings are also consistent with a synchronous process. Although the evidence points strongly toward a synchronous process in the case of the cyclization *(89)*→*(90)*, it should be emphasized that this result does not constitute proof that all cationic polyene cyclizations are synchronous.

7. Conclusion

Acid-catalyzed biomimetic polyene cyclization of acyclic chains is a viable synthetic tool for the stereospecific formation of polycyclic systems. Acetal as well as allylic alcohol functions are useful initiators for these cyclizations, and methylacetylenic end groups are particularly useful terminators which can give exclusive five-membered ring formation, and thus make possible the total synthesis of the steroid nucleus in a single step starting from a one-ring substrate.

The stereochemical course of natural, enzymic polyene cyclizations may to some extent be guided by the same effects that seem to control the non-enzymic processes, *i.e.*, the course of the reaction results from *trans-anti-parallel* electrophilic addition to the olefinic functions according to the prediction of *Stork et al.*[3a] and *Eschenmoser et al.*[3b].

Special thanks are due to my numerous collaborators who have made many significant contributions to the planning of this research endeavor, and who were completely responsible for its reduction to practice. I wish also to thank the National Institutes of Health and the National Science Foundation who have afforded the major financial support to our program.

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Bacteriorhodopsin as an Example of a Light-Driven Proton Pump[**]

By Dieter Oesterhelt[*]

Apart from the long known visual pigments, another retinal protein complex exists in nature, *viz.* bacteriorhodopsin from halobacteria. In contrast to the visual pigments such as the rhodopsins, which act as light sensors in the eye, bacteriorhodopsin actually transforms light energy. This energy conversion is connected with the asymmetric incorporation of bacteriorhodopsin in the lattice structure of the purple membrane which forms patches on the cell surface of halobacteria. Alongside the chlorophyll system, the purple membrane system represents the second light energy conversion principle to be discovered in living nature. Bacteriorhodopsin acts as a light-driven proton pump or as the main component of such a pump system. Absorption of light triggers off a cycle of reactions coupled with the spatially oriented uptake and release of a proton. In the intact cell an electrochemical gradient is thus built up across the cell membrane of the bacterium in which part of the absorbed light energy is stored and which is not dependent upon redox processes as in the case of respiration or photosynthesis. This electrochemical gradient can supply the energy required for ATP synthesis in the cell; a reversible proton-translocating ATPase serves as catalyst system.

1. Introduction

The questions of biological conservation and conversion of energy have long played an important role in bioenergetics. The universal storage form of energy is adenosine triphosphate (ATP)[1]: it stores chemical energy in the form of a high phosphate transfer potential and the free energy of hydrolysis of its phosphoric anhydride bonds serves to drive endergonic processes in the cell, for instance the biosynthesis of endogenous substances and the energy-dependent uptake of nutrients and salts against prevailing concentration gradients. Two pathways have hitherto been known for energy storage by ATP synthesis:

1) Substrate level phosphorylation of adenosine diphosphate (ADP) and

2) electron transport chain phosphorylations (oxidative and photophosphorylation) of ADP.

During energy storage by substrate level phosphorylation, enzyme-catalyzed reactions raise the phosphorylation potential of organic phosphates until ADP can be phosphorylated. The energy required for this kind of ATP formation is supplied by the free energy of *intra*molecular redox reactions, *e.g.* in lactic acid fermentation where one mole of glucose is transformed into two moles of lactate.

In contrast, energy storage by oxidative phosphorylation involves transfer of the electrons of an oxidizable substrate, *e.g.* lactate, *via* a chain of intermediate carriers—termed a respiratory chain—to atmospheric oxygen. Thus here too, redox energy is transformed into the free energy of formation of a phosphoric anhydride bond in the ATP molecule, but *via inter*molecular processes. The way in which ATP synthesis is coupled to oxidation of a substrate molecule has not yet been completely elucidated. In photophosphorylation (*e.g.* in bacteria), light absorption in a chlorophyll molecule effects release of an electron which then finds its way back to the chlorophyll *via* an electron transport chain resembling the respiratory chain. Again, phosphorylation of ADP is coupled to this electron flow. It is called cyclic photophosphorylation.

The bacteriorhodopsin system, the subject of this paper, differs from the previously known types of biological energy storage. Neither the raising of a phosphorylation potential nor a transport of electrons is coupled to its light energy converting function. All available evidence indicates that the absorbed light energy is not initially transformed into redox energy but directly into the energy of an electrochemical gradient which then drives the ATP synthesis. Before going into details about bacteriorhodopsin as a light-driven proton pump, we shall first consider the fundamental difference between substrate level phosphorylation and electron transport chain phosphorylation.

2. Pathways of ATP Formation

The formation of phosphoenolpyruvate *(2)* from 2-phosphoglycerate *(1)* by dehydration and subsequent ATP formation with liberation of pyruvate *(4)* (Fig. 1) may be cited as an example of substrate level phosphorylation. The high phosphorylation potential of phosphoenolpyruvate arises from the proclivity of the nascent enol form *(3)* of the pyruvate to transform into the keto form *(4)*. The free energy of hydrolysis of ATP is 7 kcal/mol, but that of phosphoenolpyruvate 12 kcal/mol.

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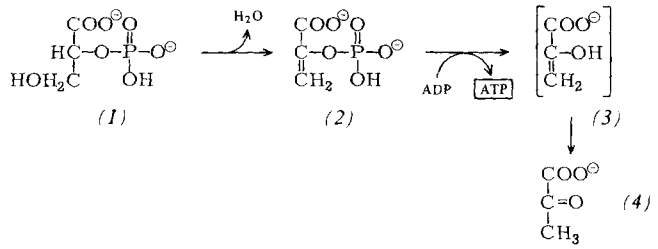


Fig. 1. Formation of ATP from phosphoenolpyruvate (2) and ADP as an example of substrate level phosphorylation.

While the substrate level phosphorylation can be described in terms of familiar transparent reactions, this does not hold for oxidative or photophosphorylation. In the latter cases, ATP synthesis is coupled to electron transport processes which are driven by light or by the negative redox potential of organic compounds. Just how this redox energy is converted into the free energy of hydrolysis of the ATP molecule is the topic of three hypotheses (Fig. 2).

According to the conformational hypothesis, conformational changes are coupled with the redox state in the case of some proteins participating in electron transport chains, *e.g.* cytochromes. As in the chemical hypothesis, a protein-phosphate compound should again have a higher phosphorylation potential in the oxidized than in the reduced state and can therefore phosphorylate ADP.

The third hypothesis, which is nowadays steadily increasing in favor, is the chemiosmotic hypothesis due to *Mitchell*[2]. He assumes that the energy liberated on oxidation of the organic substrate is transformed into an electrochemical gradient between the interior and exterior of the cell, *i.e.* in contrast to the other two hypotheses there is no chemically detectable intermediate between oxidation of the substrate and formation of ATP from ADP and inorganic phosphate. This reaction takes place on an enzyme complex which catalyzes formation of the phosphoric anhydride bond while destroying the electrochemical gradient.

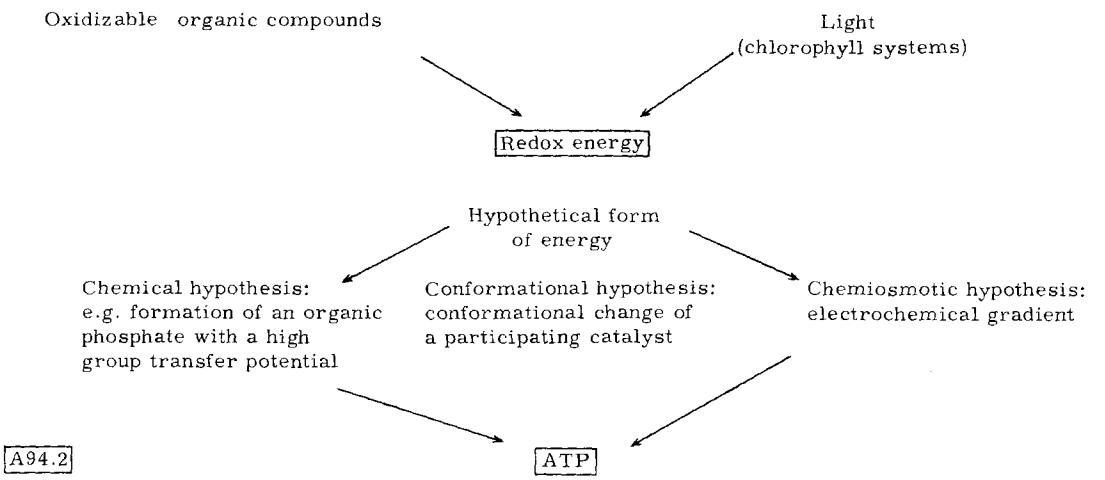


Fig. 2. Hypotheses concerning electron transport chain phosphorylation.

The "chemical hypothesis" states that organic phosphates change their phosphorylation potential simultaneously with their redox state and thus become able to phosphorylate ADP.

Figure 3 shows the requirements for conversion and storage of energy according to the chemiosmotic hypothesis. All electron transport chain phosphorylations occur exclusively on membranes: on the cell membrane in bacteria and on the

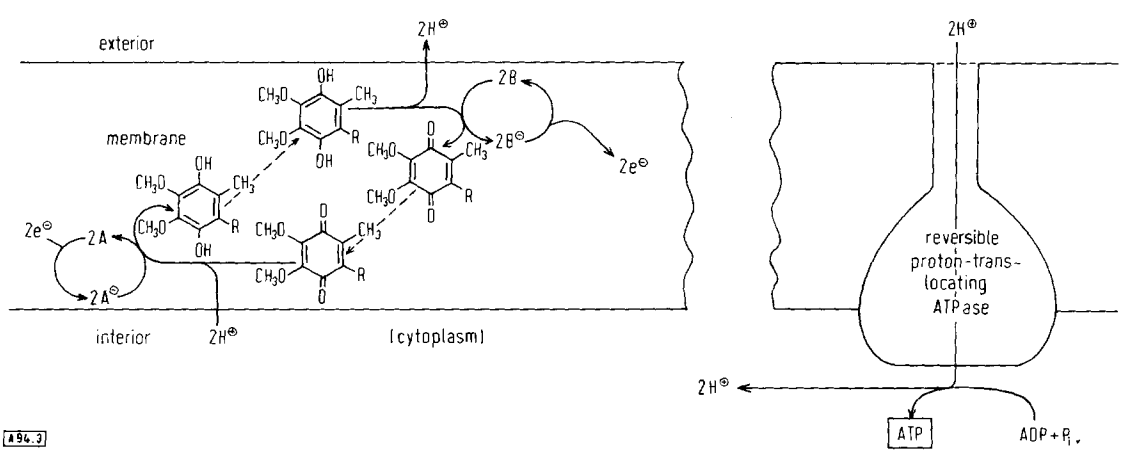


Fig. 3. Example of an electron transport chain phosphorylation (according to *Mitchell*'s chemiosmotic hypothesis, see text for details). Essential conditions are: 1) Presence of a separating membrane; 2) asymmetric distribution of catalysts (A, B) in the membrane; 3) presence of diffusible proton transporters (in this case ubiquinone = coenzyme Q). The dashed arrows between the two (identical) quinone and hydroquinone molecules are intended to indicate the diffusion of these molecules.

inner mitochondrial membrane in higher cells. A membrane is most simply defined as a lipid-protein mixed phase, which separates two aqueous reaction spaces and is semipermeable. The catalysts (A, B) of the electron transport chain are distributed asymmetrically in this phase, *i.e.* they lie more toward the interior or more toward the exterior reaction space. Also of importance is the presence of diffusible "proton transporters" such as quinones and hydroquinones in the membrane. Figure 3 shows a section of an electron transport chain in which—going from left to right—electrons reduce a catalyst A on the "inside" of the membrane to A^-. This ion is reoxidized by a quinone, which, to this end, takes up two protons from the cytoplasm and is converted into the corresponding hydroquinone. The hydroquinone diffuses freely through the membrane and can thus be reoxidized to the quinone by B, a second catalyst in the respiratory chain, on the "outside" of the membrane. Two protons are released to the external medium, and the quinone returns to the cycle. The electrons are transported *via* further intermediate catalysts to the final electron acceptor, frequently oxygen. However, some organisms also utilize nitrate, sulfate, or even organic substances for this purpose. Hence, Figure 3 illustrates that section of a two-electron transfer with which transport of two protons out of the cell through the membrane to the exterior is strictly coupled.

Now what is the result of this proton transport? If the membrane were impermeable to ions, the change in redox potential during oxidation of a substrate would be completely transformed into a membrane potential. This membrane potential is the electrostatic field built up by the transported protons. Such potential differences between the interior and exterior of a cell can reach about 300 mV. Bearing in mind that the charges are separated only by the *ca.* 30 Å—thick lipid phase of the membrane, we see that the field strengths must be of the order of 100000 V/cm, *i.e.* extremely high.

Let us now consider a second non-ideal case in which the cell membrane is hardly permeable to protons but more permeable to other cations, *e.g.* potassium ions. This permeability is due to passive diffusion and can be enhanced by ion transporters like cyclic antibiotics or natural carriers (facilitated diffusion). The driving force for the influx of potassium ions (or other cations) is always the electrostatic field generated by the electron-transport driven proton pump. Depending upon the permeability conditions in the separating membrane, the chemical potential of the protons pumped out

$$\Delta\mu_{H^+} = F\Delta\psi - 2.3RT\Delta\,(\mathrm{pH})$$

will be distributed to differing extents between two quantities, *viz.* the membrane potential (electrostatic field) and the concentration gradient. According to the chemiosmotic hypothesis, the electromotive force is thus converted into a "protonmotive" force

$$\Delta p = \Delta\psi - Z\Delta\,(\mathrm{pH})\,[\mathrm{mV}]; \quad Z = 59$$

which supplies the free energy required for ATP synthesis in the cell interior. To this end, the protons previously pumped out are channeled back into the cell by an enzyme system, called reversible proton-translocating ATPase, with concomitant ATP synthesis (Fig. 3). The overall process of energy storage thus comprises two partial steps:

1) Protons are channeled out of the bacterial cell in a pumping action driven by redox processes and build up a potential gradient.

2) The energy of the returning protons is utilized for the enzymatic synthesis of adenosine triphosphate.

Table 1. Some ATPases whose common catalytic property is the coupling of the electrochemical potential of an ion with the ATP hydrolysis/synthesis equilibrium.

Name	Occurrence	Function
Ca^{2+} ATPase	sarcoplasmic reticulum (muscle)	regulation of Ca level in muscle
Na^+/K^+ ATPase	cell membrane, *e.g.* nerve cells	maintenance of high intracellular K level
H^+ ATPase	mitochondria, bacteria	ATP synthesis

Reversible translocating ATPase is not the only enzyme able to couple an electrochemical gradient with the synthesis and hydrolysis of ATP[2a]. ATP synthesis at the expense of an ionic gradient has been established for both the "calcium pump" of the sarcoplasmic reticulum in muscle and the "sodium-potassium pump" in plasma membranes. However, viewed physiologically, it is the task of the calcium and the sodium-potassium pump to generate an ionic gradient by ATP hydrolysis, but that of the proton pump to exploit such an ionic gradient for ATP synthesis (Table 1). The enzymatic mechanism of the energy coupling is one of the central unsolved problems of biochemistry. Nor has the mode of operation of the proton pump driven by electron transport yet been elucidated.

Let us now return to the bacteriorhodopsin system! Like the electron transport chain of photosynthesis, bacteriorhodopsin can be described as a light-driven proton pump which, embedded in the cell membrane, also builds up an electrochemical gradient that is exploited for ATP synthesis in the cell[3]. Nor is the source of primary energy new in this system—it is simply light as in the case of green plants or photosynthetic bacteria. What is new is the mode of action of this pump, for it is not dependent on a flow of electrons. A cycle of conformational changes of bacteriorhodopsin following light absorption is responsible for the pumping action on protons.

3. Occurrence, Isolation, and Structure of the Purple Membrane

Halobacteria, in which bacteriorhodopsin is found, are truly remarkable organisms. These bacteria live only in common salt solutions of maximum concentration and even survive in crystalline salt. They were discovered in Scandinavia around the beginning of the century on dried salted fish which was considered to be spoilt on account of its reddish color[4].

In seawater basins for salt production or evaporating lagoons, *etc.*, halobacteria reach high cell population densities which give rise to extensive red coloring as a result of their carotenoid pigments. Exceptional properties are the rule for these bacteria. Thus they possess a cell wall made up exclusively of protein aggregates. The cells have a diameter of about 0.5 μm and a length of 5—10 μm. On viewing the cell surface after removal of the wall by freeze fracturing, the cell membrane does not appear to be homogeneous but instead bears patches

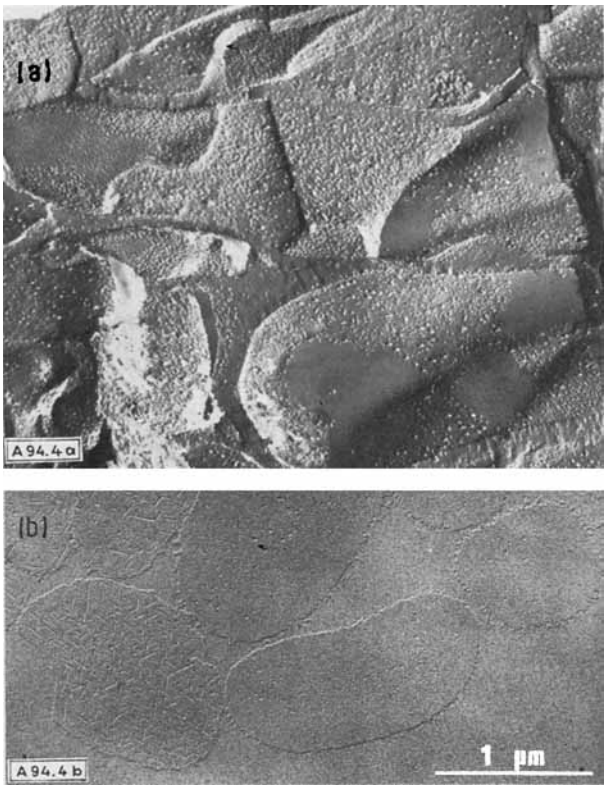


Fig. 4. Electron micrograph of purple membrane patches (*Halobacterium halobium*). a) Purple membrane patches in intact cells. The surface of the patches appears smooth or rough depending upon whether the inside or the outside of a cell is being shown. At the same time, a pronounced structural asymmetry of the membrane patches is to be seen (according to ref. [7]). b) Isolated purple membranes after spraying onto freshly cleaved mica and shadowing with platinum/carbon (photograph by *M. Clavier*).

of about 0.5 µm in diameter (Fig. 4a). Fortunately, these patches can be isolated preparatively and studied *in vitro*: if halobacteria are exposed to pure water, the cells lyze and the cell membrane fragments can be separated by simple centrifugation techniques[5, 6].

The heaviest fraction has a deep purple color and is therefore called the purple membrane fraction. It consists of membrane sheets having a diameter of about 0.5 µm. Physical studies by *Blaurock* and *Stoeckenius* have revealed that this fraction actually comprises the above-mentioned patches which are scattered over the cell membrane as differentiated regions[7]. This purple membrane is composed of 75% protein and 25% lipid. The protein component consists of a sole species, bacteriorhodopsin, whose molecular weight is about 26000 daltons (Fig. 4b). The difference between the inner and outer membrane surfaces is underlined by the appearance of cracks in only half of the membrane patches.

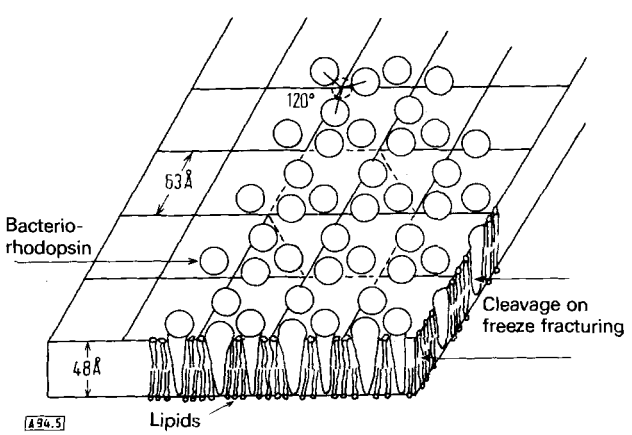


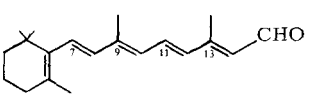
Fig. 5. Schematic representation of the purple membrane structure according to *Blaurock*, *Stoeckenius*, and *Henderson*[7–9].

Figure 5 summarizes our present knowledge about the structure of the purple membrane. Bacteriorhodopsin is arranged in groups of three molecules each at the points of a two-dimensional hexagonal lattice. The purple membrane is only about half as thick as other membranes; like the periodic arrangement of the protein, this also emphasizes that the purple membrane is by no means a normal biological membrane. As hinted in Figure 5, the protein molecules span the entire cross-section of the membrane or at least a considerable part thereof; each bacteriorhodopsin molecule is markedly asymmetric and all these molecules are oriented in the same direction. Very recent investigations by *Blaurock* and *Henderson* have shown that a considerable part of the protein is present in helical form and that these helices are arranged perpendicular to the plane of the membrane[8, 9]. The non-uniform distribution of the protein over the two surfaces of the membrane—about two-thirds on one side and one third on the other—can be demonstrated by freeze fracturing and observation of the replicas in an electron microscope. The hexagonal structure of the purple membrane can also be rendered visible by adsorbing membrane patches on *e.g.* mica, drying, and shadowing with platinum/carbon. On shrinking, the membrane cracks along the hexagonal edges; this follows from the observation that the cracks run parallel to each other or at angles of 60 or 120° (cf. Fig. 4b).

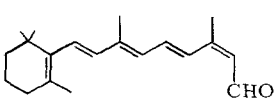
Summarizing, it may be said that bacteriorhodopsin is organized asymmetrically in the cell surface of the bacterium in the form of periodically arranged aggregates, and that this uniform orientation in the membrane structure is an essential prerequisite for the proton pumping action of the molecule.

4. The Chromophore of Bacteriorhodopsin and Its Photochemical Cycle

Halobacterium halobium is the only bacterium in which vitamin A aldehyde (retinal) has so far been detected. This substance otherwise occurs only in organisms having the power of vision.



all-*trans*-retinal



13-*cis*-retinal

Retinal, which exhibits an absorption maximum in the near UV at 380 nm, is covalently bound to the protein bacterioopsin in bacteriorhodopsin. Through interaction with its amino acid side chains, retinal forms a chromophore with the protein; the absorption maximum shows a considerable red shift, occurring at 560 nm, and is responsible for the purple-violet color of the membrane (Fig. 6). The chemical structure of this chromophore is unknown. It is called purple complex and also appears in a test tube on mixing of retinal and bacterioopsin. The specificity is very pronounced; only 13-*cis* and all-*trans* retinal afford the chromophore[10].

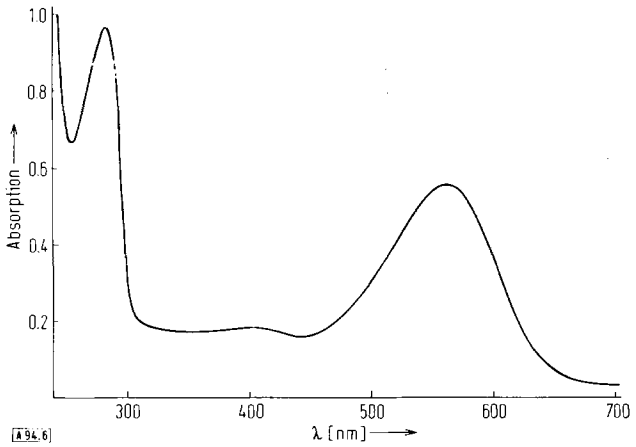


Fig. 6. Absorption spectrum of the purple membrane.

This clearly differs from the visual pigments, whose chromophore can only be formed with 9-*cis*- or 11-*cis*-retinal, *i.e.* the physiological retinal isomer. As light sensors, the visual pigments have a completely different function from the light transducer bacteriorhodopsin; this could be due to the presence of different retinal isomers.

The primary photochemical reactions in the visual pigments and in bacteriorhodopsin are similar. The light quantum absorbed by the chromophore induces changes not only in the chromophore itself but also in the surrounding protein structure. This conformational change triggers the visual process in the case of the visual pigments; in bacteriorhodopsin it leads to a product which regenerates the original chromophore within milliseconds, *i.e.* bacteriorhodopsin is subject to a thermoreversible photochemical reaction. Visual pigments do not display this thermoreversibility. This difference is most probably due to the presence of 11-*cis*-retinal as a component of these retinal-protein complexes. Light induces the isomerization of the thermodynamically unstable (because sterically hindered) 11-*cis* compound to the all-*trans* form which is unable to regenerate the original chromophore. Only an external supply of 11-*cis*-retinal leads to regeneration of the visual pigment rhodopsin[11].

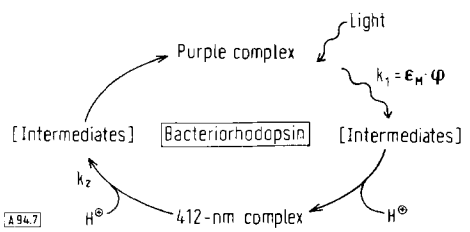


Fig. 7. Photochemical cycle of bacteriorhodopsin.

Figure 7 shows the thermoreversible photochemical reaction of bacteriorhodopsin as a cycle and emphasizes two particular states of the chromophore or the chromoprotein: the purple complex (or 560-nm complex) and the 412-nm complex. Absorption of light by the purple complex ($\varepsilon_M = 63000$) leads with a quantum yield (φ) of about 0.8 *via* one or more intermediates to the 412-nm complex, the longest-lived intermediate of the cyclic reaction sequence. From there, a reaction leads back to the starting state.

Under appropriate irradiation conditions the purple complex and the 412-nm complex form a quasi-steady state mixture whose spectral characteristics can be recorded in a rapid scan spectrophotometer. Figure 8 compares the absorption bands of the two chromophore states. Even if more than two states of the protein are involved in the photochemical cycle of bacteriorhodopsin (B), the rate constants of the formation and decomposition of the longest-lived intermediate (412-nm complex) suffice for derivation of the rate law of this reaction cycle:

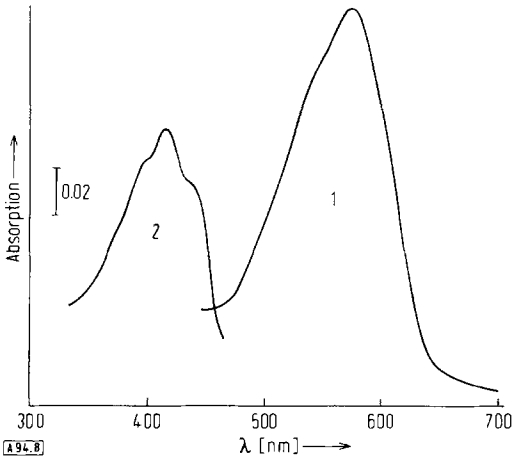


Fig. 8. Absorption bands of the bacteriorhodopsin chromophore in two different states (frozen at −196 °C): 1) purple complex in the dark. 2) the longest-lived intermediate (412-nm complex) of the photochemical cycle in the light.

$$V = \frac{k_2\,[B]}{1 + k_2/\varepsilon\varphi J} \qquad V_{max} = k_2\,[B]$$

$$k_1 = \varepsilon_M \varphi$$

The rate of decay of the 412-nm complex is determined only by its own concentration, whereas the rate of its formation depends upon the light intensity (J) and the concentration of the purple complex. The situation resembles a classical Michaelis-Menten relation between the rate of an enzymatic reaction and the substrate concentration: in the case of bacteriorhodopsin (B) the substrate concentration is replaced by the light intensity. If the intensity is increased the rate of reaction increases until it reaches a constant value k_2 [B] which is independent of light intensity (but dependent upon temperature). This is analogous to the turnover number of an enzyme and can be determined experimentally as k_2. Accordingly, the cycle is found to be repeated about 200 times per second in bacteriorhodopsin at room temperature and light saturation.

Two further properties of the photochemical cycle also deserve mention in this context. Under natural illumination conditions the cycle is light-limited, *i.e.* it does not attain its maximum rate. Moreover, there is a photochemical retroreaction leading from the 412-nm complex to the purple complex[12].

Under suitable experimental conditions the different properties of the purple complex form and the 412-nm complex form of bacteriorhodopsin can be determined[13]. These are:

1) Differing tryptophan fluorescence, indicating conformational differences between the two forms.

2) Differing reactivity of the chromophore toward hydroxylamine and hydridoborate. Only the 412-nm complex (or one of the other intermediates) reacts *via* liberation of retinal oxime or irreversible fixation of a retinyl group to the protein.

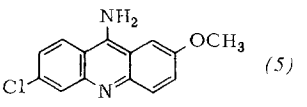
This behavior can be attributed to a differing spatial arrangement of the protein in the environment of the chromophore and/or a change in the electronic structure of the chromophore. In this connection. the difference between the spectra of the two forms is remarkable (cf. Fig. 8). While the purple complex displays the typical spectrum of a retinal compound, the 412-nm form has a three-peak spectrum typical of *retro*-retinals[12], *i.e.* retinals in which the double bonds are shifted by one position.

3) Differing energy content. Part of the light energy absorbed is stored in the 412-nm complex, as is evident from its complete transformation into the purple complex in the dark.

4) Differing p*K* values. Of crucial importance for the function of bacteriorhodopsin as an ion pump is the shift in p*K* values of the protein on going from one form to the other. Protons are liberated on transition to the 412-nm complex, and taken up again on regeneration of the purple complex.

The photochemical cycle of bacteriorhodopsin is thus accompanied by successive release and uptake of a proton. The light energy absorbed, amounting to some 50 kcal/mol, is distributed between the bacteriorhodopsin and the proton. Part of it is transferred to the 412-nm complex and drives the photochemical cycle, while the remainder permits the proton to build up the electrochemical gradient. We may further expect the proton to leave the protein molecule at a site other than that reserved for uptake of the next proton, in other words that each individual bacteriorhodopsin molecule (or possibly, even a defined association of protein and lipid) is a molecular pump. However, a net proton transfer will only be observed if the bacteriorhodopsin molecules are not arranged randomly but all possess the same orientation as in the cell membrane.

The situation in the cell can be simulated by a very simple artificial system which permits the study of bacteriorhodopsin as a proton pump. *Racker* and *Stoeckenius* were the first to show that the purple membrane can be incorporated into lipid films in such a manner that the orientation of bacteriorhodopsin is retained in a system that can form a vesicle (proteoliposome) enclosing a volume separated from the solution and thus serving as a model for a cell[14]. On irradiation of such proteoliposomes the external medium becomes alkaline, *i.e.* the bacteriorhodopsin pumps protons into these vesicles. When the light is switched off, the protons flow back out of the vesicles so that the pH of the external solution returns to its original value (Fig. 9a). Since these protein lipid vesicles are too small to permit pH measurement in their interior we have to resort to an indirect method of establishing the pH gradient. This can be accomplished with fluorescing amines[15] whose unprotonated form can easily penetrate the lipid wall of the vesicles while the protonated cannot do so. Amines such as 9-amino-6-chloro-2-methoxyacridine *(5)* are therefore distributed between the inner and outer phase in accord with the pH gradient. It was shown for chloroplasts and liposomes that the fluorescence of the dye accumulating in the interior is completely suppressed and that the extent of fluorescence suppression is a measure of the resulting pH gradient. The finding shown in Figure 9b confirms our prediction that bacteriorhodopsin transports protons into the interior by a pumping action and that the acridine derivative accumulates. On irradiation the fluorescence of the added dye *(5)* is extinguished; it reappears when the light is switched off.



(5)

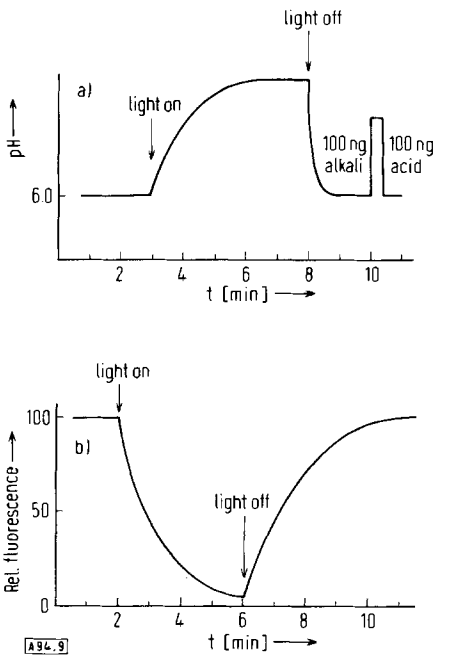


Fig. 9. Demonstration of a light-generated pH gradient with lipid vesicles (proteoliposomes) containing bacteriorhodopsin. a) Reversible pH increase of the exterior medium on illumination (ΔpH $\approx$ 0.1). b) Reversible change in fluorescence of the acridine dye 9-amino-6-chloro-2-methoxyacridine *(5)* in the interior of a lipid vesicle on illumination. Bacteriorhodopsin: 5×10^{-7} mol/l; *(5)*: 2×10^{-6} mol/l.

A pH gradient of the size shown in Figure 9a (ΔpH $\approx$ 0.1) can only arise if the inward pumping of protons is accompanied by an efflux of other cations or an influx of anions. As mentioned in Section 2, this counter-transport can be due to the permeability of the separating layer. However, it could also be an inherent property of the pump molecule, *i.e.* bacteriorhodopsin could take up a potassium ion, for instance, for each proton released in its photochemical cycle. Bacteriorhodopsin would then be a light-driven ion exchanger having a neutral pump effect, *i.e.* the potential component of the proton-motive force generated by the pump would always be equal to zero. We can, however, be sure that bacteriorhodopsin is not an electrically neutral pump of this kind but rather an electrogenic pump, *i.e.* that the photochemical cycle is accompanied only by the cyclic release and uptake of protons. On the one hand, the build-up of the pH gradient and suppression of fluorescence by the pump are limited by a slower process, *e.g.* counterdiffusion of a cation. On the other hand, *Skulachev et al.* have incorporated bacteriorhodopsin into planar lipid films separating two compartments of aqueous electrolyte solutions and succeeded in generating (and measuring) potentials of up to 300 mV in this system by irradiation[16]. Summarizing, we may say that bacteriorhodopsin acts as an electrogenic pump for protons with a turnover number of about 200 s^{-1}.

5. Energy Conversion in the Intact Cell

In the intact cell bacteriorhodopsin is oriented in the opposite direction compared to the situation in proteoliposomes, *i.e.* protons are pumped out of the cell (Fig. 10). It can be

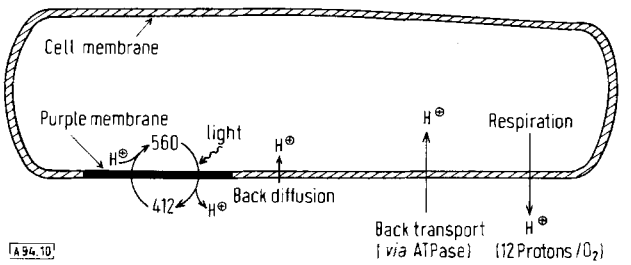
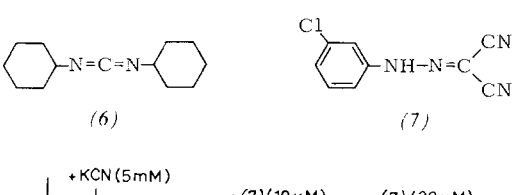


Fig. 10. Schematic representation of the proton translocating events in the halobacterium cell. 412 = 412-nm complex; 560 = purple complex.

calculated from the turnover number, the bacteriorhodopsin concentration of the cell (about half the cell surface is covered by purple membrane), and the volume of a cell that, given light-saturation, a proton-motive force of about 300 mV can be generated within a millisecond, a value sufficing for ATP synthesis. All other ion flows observed so far are slower, including the passive back-diffusion of protons without performing any work. Thus bacteriorhodopsin-driven ATP synthesis can start-up immediately, but must satisfy a number of requirements: inhibitors of ATPase such as dicyclohexylcarbodiimide *(6)* or uncouplers (substances which drastically raise the permeability of the cell membrane to protons) must suppress the photophosphorylation of the cells. Furthermore, competition is also expected between the light-driven proton pump bacteriorhodopsin and the electron transport-driven proton pump. The two proton pumps do indeed compete; quantitative comparison of absorbed quanta and unconsumed oxygen shows that not only the photochemical cycle of bacteriorhodopsin, but also the energy conversion within the cell under physiological conditions, proceed with a high quantum yield[17].



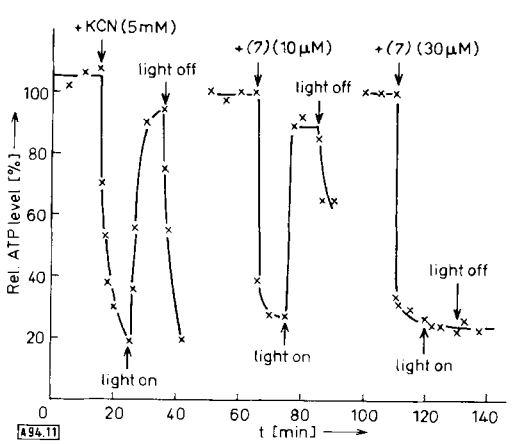


Fig. 11. Effect of cyanide and the uncoupler *m*-chlorophenylhydrazonomalononitrile *(7)* on photophosphorylation in halobacteria (according to ref. [19]).

Photophosphorylation[18, 19] can be detected in halobacteria under anaerobic conditions or after respiratory poisoning by cyanide. Figure 11 shows how added potassium cyanide (5 mmol/l) lowers the intracellular ATP level from 100 to about 20 %, since oxidative phosphorylation is inhibited and substrate level phosphorylation is not operative under the conditions given. If the light is now switched on the ATP level rises to almost the same value as that attained on maximum respiration. Since the halobacteria do not contain chlorophyll this is a new type of phosphorylation. If an uncoupler, *e.g. m*-chlorophenylhydrazonomalononitrile *(7)*, is added to the respiring cells in a further experiment, then at a concentration of 10 µmol/l the respiration is rendered inefficient as an electron-transport driven pump, *i.e.* the ATP level falls because protons no longer synthesize ATP on translocating ATPase but undergo passive diffusion through the now permeable cell membrane, *i.e.* without performing any work. Evidently being a more efficient pump, bacteriorhodopsin can pump the protons out of the cell faster than they can flow back in passively and hence the ATP level returns almost to the original value on irradiation. If the concentration of uncoupler is raised to 30 µmol/l and the permeability of the membrane thus increased still further, the cell ATP level can no longer be enhanced by irradiation.

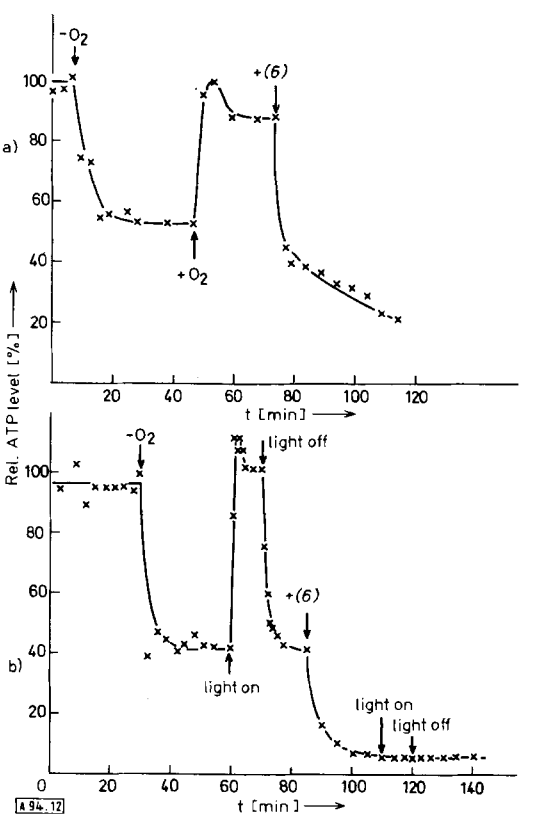


Fig. 12. Comparison between oxidative phosphorylation (a) and photophosphorylation (b) in halobacteria. As inhibitor of reversible proton translocating ATPase, dicyclohexylcarbodiimide *(6)* renders the cells incapable of ATP synthesis in both cases (according to ref. [19]).

Figure 12a illustrates the inhibition of the ATP-synthesizing system by dicyclohexylcarbodiimide *(6)*. Oxygen is first withdrawn reversibly from the cells and the oxidative phosphorylation then inhibited irreversibly by addition of *(6)*. Figure 12b shows the drop in ATP level after switching off the oxygen and the rise in the ATP level on irradiation. Addition

of *(6)* after switching off the light and subsequent irradiation no longer change the ATP level—the pump has been chemically uncoupled from ATP synthesis.

Another prediction arising from the scheme shown in Figure 10 is the interaction of the proton pump with the return transport of protons by the ATPase system. Expectedly, the initial rate of ATP synthesis increases with increasing light intensity since the pumping rate of bacteriorhodopsin also increases with the light intensity. This can continue until the process is limited by the ATP-synthesizing system; the rate of ATP synthesis then remains constant.

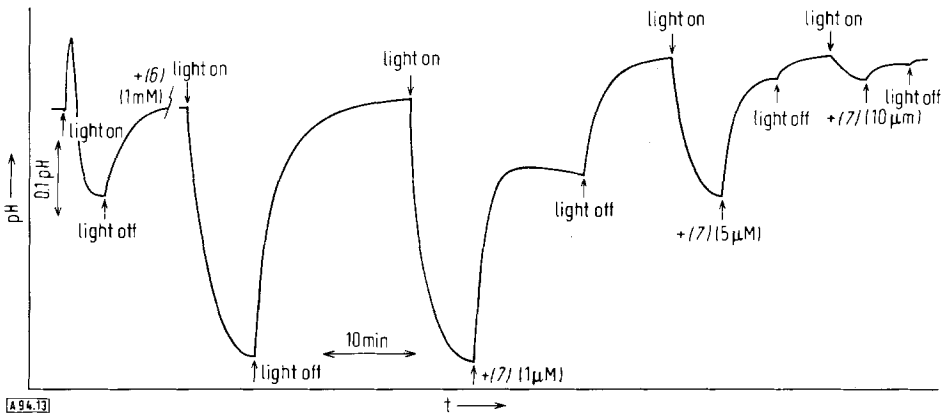


Fig. 13. Uncoupling of the light-driven proton pump from ATP synthesis by dicyclohexylcarbodiimide *(6)* and the increasing drop in efficiency of the proton pump with progressive addition of the uncoupler *m*-chlorophenylhydrazonomalononitrile *(7)* (according to ref. [19]).

That bacteriorhodopsin functions as a light-driven proton pump can also be demonstrated in the cell after inhibition of ATP synthesis. The complicated interplay of the proton pump and ATP level with regard to the pH values in the external medium will not be considered here. If ATP synthesis is uncoupled by dicyclohexylcarbodiimide *(6)* then the action of the proton pump can be studied by itself (Fig. 13). An equilibrium pH is established in the light; its value depends upon the pumping rate and the passive back diffusion of protons. This pH difference of the medium in the light and in the dark becomes increasingly smaller on addition of *m*-chlorophenylhydrazonomalononitrile *(7)* until the cell membrane has become completely permeable to protons.

6. Outlook

In conclusion it should be emphasized that the action of bacteriorhodopsin as a light-driven proton pump can be established and understood both for artificial systems and for the intact cell. However, to this day the chemistry of the chromophore change effecting vectorial expulsion of a proton has defied all attempts at elucidation. It is certainly a challenging task to develop model concepts, say on the basis of retinal-*retro*-retinal transitions, which are able to explain such a process. This would be the first explanation of an active transport process on a molecular level. However, even greater difficulties impede our understanding of how an electrochemical gradient extending across a cell membrane can shift a chemical equilibrium and what enzymatic reactions are involved. This central problem of bioenergetics will undoubtedly require a much longer time for its solution.

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Far-Infrared Fourier Spectroscopy as a Method for Structure Determination in Chemistry

New analytical methods (4)

By Erich Knözinger[*]

Couched in the often confusing term "Fourier Spectroscopy" is the combined exploitation of a fundamental physical concept, a simple mathematical principle, and use of modern data technology. Introduction of this relatively young method into instrument technology has given great impetus to nuclear magnetic resonance and infrared spectroscopy. The infrared spectroscopic investigation of low frequency molecular vibrations has especially profited; in this connection one speaks of far infrared (FIR) Fourier Spectroscopy, which has opened up numerous interesting applications in organic, inorganic, and physical chemistry.

1. Introduction

Nowadays, the methods of vibrational spectroscopy—IR and Raman spectroscopy—are used along with NMR and mass spectroscopy for the elucidation of chemical structures[1, 4]. In principle they afford an almost complete overview of the vibrational behavior of molecules, from which structural parameters can be determined qualitatively and quantitatively. The two methods are distinguished by the complementary nature of the information which they provide. Vibrations accompanied by a strong change of dipole moment can be observed particularly well in the IR spectrum (intense IR absorption bands); vibrations accompanied by a strong change in polarizability are readily observed in the Raman spectrum (intense Raman lines). If a molecule has a center of symmetry the vibrations are observable either in the IR spectrum only (exclusively IR-active vibrations) or in the Raman spectrum only (exclusively Raman-active vibrations). However, the ideal case for vibration-spectroscopic analysis, in which the frequencies of all normal vibrations of a molecule can be determined, seldom occurs. The reasons for this are far less theoretical than practical ones—equipment parameters and methods of sample preparation effect reduction in information quality, particularly in the region of low frequency vibrations. In the first place more or less pronounced difficulties are met with—depending on the measuring principle in the IR spectroscopic investigation of low frequency vibrations—due to the smallness of the signals to be measured. In this connection the Fourier method or Fourier spectroscopy as a measuring principle has enabled considerable advances to be made over the conventional dispersive methods. One refers to the spectral region of electromagnetic radiation, which on the one hand embraces the low frequency vibrations and on the other is a region in which the advantages of the Fourier method become particularly apparent, as the far IR or FIR region. Its upper and lower limits lie at *ca.* 500 cm^{-1} (20 μm; 1.5×10^{13} Hz) and 10 cm^{-1} (1000 μm; 3.3×10^{11} Hz), respectively. In the present review the types of vibrations to be expected in the FIR region are first briefly characterized. The wealth of structural information which they disclose seems to justify the considerable outlay on apparatus necessary for making the FIR region accessible. Currently one already has the choice of half a dozen commercially available FIR apparatus. They all function, with one exception, on the same measuring principle: the Fourier method. In order to provide a fully illustrative account of this measuring principle and its more important consequences the following review will deal with the most striking advantages of the Fourier method in the FIR region as well as the fundamental principles that it has in common with conventional dispersive methods.

2. Applications of FIR Spectroscopy in Chemistry

What is the information that can be derived from the FIR spectrum of a specific substance? It comprises information about the rotational and vibrational behavior of molecules. In this field the main accent is laid on vibrations since only a very few small molecules such as H_2O, D_2O, H_2S, CO, NH_3, HCl, *etc.*[6, 7] show pure rotational transitions in the FIR region. Apart from these exceptions the typical spectral region for pure rotational transitions is the microwave region. (For gaseous samples rotational transitions can of course be superimposed[5] on vibrational transitions.)

If we assume a harmonic oscillator the frequency $\tilde{\nu}$ (measured in cm^{-1}) of the vibration of a diatomic molecule can be calculated from the relationship:

$$\tilde{\nu} = \frac{1}{2\pi c}\sqrt{\frac{k}{m_r}} \qquad (1)$$

where m_r is the reduced mass, k the force constant, and c the velocity of light. For polyatomic molecules the one vibration of the diatomic molecule is replaced by a series of so-called normal vibrations. In general the more complicated is the structure of a molecule—and here we include giant molecules such as exist in the form of crystals—the more complicated becomes the calculation of the frequencies and types of its vibrations. Equation (1) can be generalized for polyatomic molecules as follows: The frequency or the wave number of an individual normal vibration is the smaller, the greater the masses (for rotatory vibrations moments of inertia) concerned in the vibration and the smaller the forces (for rotatory vibrations torques) that oppose the displacement of individual molecular components from the equilibrium positions. On the basis of several decades of experience[*] with the assignment of MIR spectra (MIR region: 4000 to *ca.* 400 cm^{-1}) of organic and inorganic substances one can extrapolate from this generalization of relation (1) to the FIR region. One can thus predict

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[*] The first absorption spectra in the IR region were measured by *W. W. Coblentz* in 1905.

which molecules will undergo normal vibrations with frequencies in the FIR region.

The relevant types of vibration will be characterized in the following sections and explained by means of examples. The numerical values quoted for the force constants should be regarded as only approximate.

In the present progress report it will not be possible to deal with the numerous applications of FIR spectroscopy in the field of physics particularly solid-state physics. For this purpose the reader is referred to the book by *Möller* and *Rothschild*[2] which contains, *inter alia*, a review of all present-day physical applications of FIR spectroscopy.

2.1. Stretching Vibrations

Normal vibrations are described as stretching vibrations if they lead predominantly to changes in the bond lengths. This type of vibration is observed in the FIR region[9] if heavy constituents are present in the molecule and their movement actually contributes to the change in the relevant bond length. In this connection the heavy constituents are considered—naturally only as a rule—to be the elements of the fourth and higher periods of the Periodic Table. Typical examples of application are the FIR investigations of carbonyl-[10] and halo-metal complexes[11, 12].

The probability of finding a definite stretching vibration in the FIR region is further increased by two effects:

- not only the masses of the atoms but also their ionic radii increase from period to period. The larger the ionic radii of the bonded atoms, the longer is the bond length and, according to Badger's rule[8], the smaller is the force constant.
- it is often not only the masses of the atoms directly involved in a particular chemical bond but also larger masses that are effective, as is shown when under certain conditions the bonded atoms vibrate approximately in phase with the ligands attached to them. In such cases, the term skeletal vibrations is used (Section 2.3).

2.2. Bending Vibrations

Bending vibrations is the term applied to normal vibrations in which mainly the bond angles change. They occur at lower wave numbers than the comparable stretching vibrations, since the forces that oppose displacement of molecular components from their equilibrium positions are always stronger along the direction of the bond than perpendicular to this direction. Thus, bending vibrations are found in the FIR region for all compounds whose stretching vibrations are to be found in that region[9], *e.g.* carbonyl-[10] and halo-metal complexes[11, 12]. Furthermore, bending vibrations also appear in the FIR region when light atoms (elements of the second and third periods) are involved; as an example may be mentioned the bending vibration by which the COC angle in methyl formate or methyl acetate is altered (325 or 303 cm^{-1}). Still lower wave numbers are recorded if whole groups of atoms vibrate completely or approximately in phase with the atoms under consideration; this can be shown *e.g.* for alkyl formates when the alkyl group is larger than a methyl group[13]. In this case the term skeletal vibrations is also used (see Section 2.3).

2.3. Skeletal Vibrations of Macromolecules

The skeleton of macromolecules consists in general of relatively light atoms, *e. g.* carbon atoms, but it undergoes forms of vibration in which large groups of neighboring skeletal atoms vibrating in phase vibrate in opposition to other such groups. The force constant is then approximately of the same magnitude as in the stretching or bending vibrations of skeletal atoms of a comparable smaller, *e.g.* triatomic, molecule; however, in general very much larger masses are concerned, as they are—to a first approximation—the sums of the masses of atoms vibrating in phase. Correspondingly, the wave numbers for such skeletal vibrations are low.

A special case of these skeletal vibrations of macromolecules is provided by the so-called one-dimensional lattice vibrations of long-chain unbranched molecules. These include, for example, the "accordion vibration" of unbranched aliphatic hydrocarbons[14, 15], where the wave number is smaller than 220 cm^{-1} when ten or more carbon atoms are concerned; admittedly, this vibration is Raman-active only when the chain skeleton consists wholly of the same type of atoms (*e.g.* carbons) and when the substituents on the skeletal atoms are all of the same type.

2.4. Skeletal Vibrations of Ring-Shaped Molecules

The skeletal vibrations of ring-shaped molecules generally occur in the FIR region if there are only negligible changes in the bond lengths and bond angles. Such vibrations are observed in the case of planar or almost planar rings, if the ring atoms swing out of the "ring plane". In the case of four- and five-membered rings this form of vibration is known as ring-puckering vibration (cf. Fig. 1).

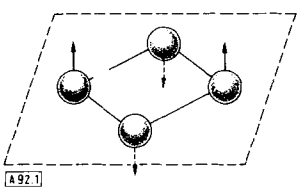

Fig. 1. Schematic representation of the ring puckering vibration of a four-membered ring (for the sake of simplicity the substituents on the ring atoms have been omitted).

In the absence of double bonds the force constant for this type of vibration is determined mainly by the interaction forces between the substituents on the various ring atoms. The magnitude of these forces is of the same order as that of intermolecular interactions; this explains the low wave numbers of ring-puckering vibrations which, for example, are observed for oxetanes between 50 and 160 cm^{-1}[16]. Immediately double bonds are present in the ring, the respective vibrations occur at higher wave numbers.

2.5. Torsional Vibrations

In torsional vibrations (as in ring-puckering vibrations) the bond lengths and bond angles also remain, to a first approximation, unchanged. What is changed is a dihedral angle (Fig. 2), *i.e.* the orientation of two parts of the molecule relative

to one another; here the only degree of freedom is the rotation of the two parts of the molecule (AX_2, BY_2) around the chemical bond (A—B) connecting them. The wave number $\tilde{\tau}$ for the torsional vibration depends on the reduced moment of inertia I_r and on the torque constant D:

$$\tilde{\tau} = \frac{1}{2\pi c}\sqrt{\frac{D}{I_r}} \tag{2}$$

Here the reduced moment of inertia is obtained from the moments of inertia of the two parts of the molecule analogously to the way in which the reduced mass of a diatomic molecule is obtained from the two individual atomic masses. Thus, not only the mass of the atoms taking part in the vibration but also their distance perpendicularly from the rotation axis is responsible for the wave number $\tilde{\tau}$.

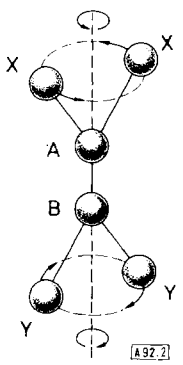

Fig. 2. Schematic representation of the torsional vibration of a molecule X_2ABY_2 around the axis of the A—B bond.

In the case of a torsional vibration around a single bond the torque constant with respect to this bond is determined by the interaction between the substituents on one of the bonded atoms (A) and those on the second atom (B); this means that its value is determined by steric factors. Typical examples are the torsion of methyl groups around C—C, C—O, or C—N single bonds[17–21, 27], the torsion of OH groups in aliphatic alcohols[22], and of NH_2 groups in primary amines[23] or hydrazines[24]. The situation is different for torsional vibrations around a bond axis that has double-bond character. The rotatability around such bonds is more restricted, and the torque constant can be determined largely by the double-bond character. As has been shown by investigations of butadiene and glyoxal and compounds derived therefrom (C—C bond axes with partial double-bond character)[25, 26] and of alkyl esters of carboxylic acids (C—O bond axes with partial double-bond character)[27], the wave numbers for the corresponding torsional vibrations depend largely on the properties of the substituents, which can exert an effect through the reduced moment of inertia and the torque constant (inductive and mesomeric effects).

2.6. Intermolecular Vibrations

The number N of normal vibrations of a nonlinear molecule composed of n atoms can be calculated from the formula:

$$N = 3n - 6 \tag{3}$$

If x molecules containing a total of $n_x = n \cdot x$ atoms come together to form an association, then N_x normal vibrations are observable where

$$N_x = 3n_x - 6$$

Together with expression (3), this gives:

$$N_x - x \cdot N = 6(x-1) \tag{4}$$

In the association there are thus $6(x-1)$ normal vibrations more than in the total of x isolated molecules. Where do these $6(x-1)$ vibrations come from?

The total number of degrees of freedom concerned with rotation, translation, and vibration is constant for a system of $n \cdot x$ atoms independently of how these atoms are combined into molecules and associations. On combination of x molecules to form an association $3(x-1)$ rotational degrees of freedom and $3(x-1)$ translational degrees of freedom disappear. An individual molecule can no longer undergo translation or rotation independently of the others; only the association as a whole has the possibility of this type of movement. These $6(x-1)$ lost rotational and translational degrees of freedom have become the above mentioned $6(x-1)$ additional vibrational (librational and translational vibrations) degrees of freedom in the association. They correspond to the so-called intermolecular vibrations in which the individual molecules vibrate as more or less rigid structures. In this process relatively large masses, namely those of the molecules, move in opposition to relatively weak forces, namely the intermolecular interactions; and this results in low-frequency vibrations generally found in the region below $300\,cm^{-1}$. The force constants have values between 1.0 and 0.001 mdyne/Å and are thus normally smaller by orders of magnitude than the force constants of principal valence bonds (*ca.* 20 to 1 mdyne/Å).

As is well known, the influence of intermolecular interactions on single molecules can be studied by various spectroscopic methods such as MIR, UV/VIS, and NMR spectroscopy. All these methods, however, have in common the feature that they supply only part of the information—they indicate how the skeleton and the electron distribution of a molecule change under the influence of specific intermolecular interactions, but information about the nature of these interactions themselves is obtained only by investigation of the lower-frequency vibrations, *i. e.* by FIR spectroscopy and Raman spectroscopy. Applications of FIR spectroscopy for such purposes are described in Sections 2.6.1 to 2.6.4.

2.6.1. Hydrogen Bonding

Association by means of hydrogen bonding is observed for water, alcohols, carboxylic acids, amines, *etc.*[28] and for their mixtures[31] with other polar compounds in the liquid and solid phase, and frequently also in the gaseous phase. The force constants for vibrations of the individual molecules in the direction of the H bonding are between 1 and 0.1 mdyne/Å; the force constants of the other so-called H-bonding "vibrations" are correspondingly smaller. Study of H bonding by FIR spectroscopy has been particularly detailed for carboxylic acids[29–30]. Intramolecular H bonding is regarded as a special case of this type of intermolecular interaction; as a kind of intermolecular interaction it is observable

in the FIR spectrum only in the form of intramolecular vibrations. Investigations of compounds of the salicylic acid type are still in progress[32].

2.6.2. "Weak" Intermolecular Interactions

Dispersive forces and dipole-dipole interactions *etc.* belong to this group. The force constants are generally smaller by 1 or 2 orders of magnitude than those for H bonding, and the wave numbers of the corresponding vibrations are therefore very low (less than $100\,cm^{-1}$)[32, 34]. Under the usual conditions the absorption bands observed are strongly broadened because of the multivarious intermolecular force constants in solid and liquid samples (cf. Fig. 3). Of particular interest in this connection are π-electron-rich (dispersive forces!) and strongly polar substances (dipole-dipole interaction!). To exhaust the information content of the FIR spectrum additional experimental work (matrix isolation technique[83]) is necessary.

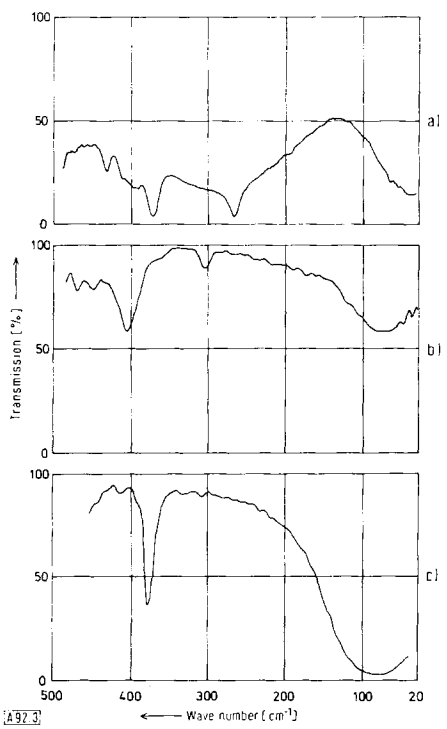

Fig. 3. FIR spectra of a) chloroform and b) benzene (liquid; layer thickness 1 mm) and c) of acetonitrile (dissolved in CCl_4, $c \approx 10$ mol-%; layer thickness 1 mm).

2.6.3. Interactions between Adsorbed Molecules and the Adsorbent

Investigation of the vibrations of adsorbed molecules with respect to the adsorbent enables some conclusions to be made about the nature of the interactions between them[35-37]. *Inter alia*, H bonding, dispersive forces, and dipole-dipole interactions may play a part here.—Such studies are important for surface chemistry and heterogenous catalysis. As examples may be cited studies on the adsorption of water[36, 37] and of organic molecules[35] on silica gel. Admittedly, the information content of the FIR spectra is usually greatly reduced because of the heterogeneity of the surface concerned and the resulting band broadening.

2.6.4. Lattice Forces in Molecular Crystals

Molecular crystals can be regarded as associations in which a very large number of molecules are joined together, whereby various types of interaction force can be observed. The intermolecular vibrations of such a crystal are known as lattice vibrations. Only those lattice vibrations in which neighboring primitive unit cells vibrate in phase can be observed by means of IR and Raman spectroscopy. This means that when the number of intermolecular vibrations of a molecular crystal observable in IR or Raman spectra is being determined, only the number of molecules combined in one primitive unit cell is taken into account; this number replaces the x in Eq. (4). In this case equation (4) must be modified further. Thus, not only the librational and translational vibrations within a primitive unit cell but also the three in-phase librational vibrations of the whole primitive unit cell around the three spatial axes can be observed in the IR and/or the Raman spectra. This is, of course, not the case for the three in-phase translational vibrations of the whole primitive unit cell in the direction of the three spatial axes; these correspond to translatory movement of the whole crystal. The number of lattice vibrations of a molecular crystal that can be observed by the methods of vibration spectroscopy thus amounts not to $6(x-1)$ [Eq. (4)], but to $6x-3$. The spectral region corresponding to these lattice vibrations lies below $200\,cm^{-1}$[33, 38].

The crystalline portions of polymers provide a special problem in crystal structure; in polyethylene, for example, the crystalline portions give rise to a lattice vibration at $72\,cm^{-1}$[39, 40].

If the masses of crystalline components are sufficiently large then, of course, also the lattice vibrations of valence and ionic crystals lie in the FIR region (*e.g.* alkali metal halides such as KBr *etc.*).

3. The Importance of FIR Spectroscopy in Chemistry and its Problems

All compounds that absorb in the FIR region exhibit absorption bands with considerably higher absorbance coefficients ε in the mid IR (MIR) and/or in the UV/VIS region; *e.g.* in the MIR region ε assumes maximum values of about $2000\,l/mol \cdot cm$, whereas the corresponding values in the FIR region are smaller by a factor of at least 1/5; naturally, this makes itself apparent, on the one hand by the amount of sample required and on the other—so as to ensure an acceptable signal-to-noise ratio in the spectrum—by increased demands on the apparatus. Even more pronounced are the differences in absorbance coefficients on comparing the FIR with the UV/VIS region. It thus follows that quantitative analyses can be carried out with very much higher sensitivity and—as regards equipment—more favorable detection limits in these shorter wavelength regions. Consequently, FIR spectroscopy is resorted to only in exceptional cases for the purpose of qualitative analysis and identification of unknown substances. Its main area of application is in structural elucidations.

Although the content of information in the FIR region is undoubtedly smaller than that in the MIR region for many compounds, in particular organic ones, the importance of the FIR region in chemistry, including organic chemistry, is not to be underestimated. The reason is that the assignment

of an FIR spectrum provides access to important physical and physicochemical information:

- The structure of many compounds that contain one or more heavy atoms can be determined with the aid of vibration-spectroscopic methods only if the FIR spectrum is taken into consideration.
- For normal coordinate analysis the information about the vibrational behavior of molecules must be as complete as possible; the low-frequency region cannot be arbitrarily excluded, for the solution is then no more than approximate.
- For determination of thermodynamic functions it is precisely the low-frequency normal vibrations that play a decisive role[41].
- Facts about the potential barriers in interconversion of conformers are closely related to the wave number of torsional and ring-puckering vibrations, which are found exclusively in the FIR region.
- Intermolecular interactions, which are often responsible for the conformation of a compound and decisively determine its physical behavior, can be investigated directly in the FIR region.

The problems of assignment in the FIR region reside in the facts that a large number of different types of vibration (see Sections 2.1 to 2.6) can be observed next to one another and that the concept of group frequencies, which so greatly assist the assignment in the MIR region, is applicable only in exceptional cases in the FIR region. The reason for this is that the low-frequency normal vibrations generally involve a relatively large number of atoms with non-negligible amplitude. This is immediately apparent for skeletal, torsional, and intermolecular vibrations; for example, in a torsional vibration around a specific bond axis there is movement of all the atoms in the molecule except those that occur along this axis. In the case of torsional vibrations one can therefore speak of a group frequency only when the reduced moment of inertia is almost identical with the moment of inertia of the group under study referred to the torsion axis; *i.e.* when this moment of inertia is small in comparison with the corresponding moment of inertia of the other part of the molecule.— An additional complication in the interpretation of the FIR spectrum arises through the increasing intensity of "hot bands" with decreasing wavelength (at 500 cm^{-1} and room temperature already *ca.* 1/10 of the molecules investigated are in the first excited state![41]) and through band-splitting which occurs, *inter alia*, in torsional vibrations and has its origin in special potential curves having two or three minima[17]. Moreover — as in the MIR region— difference bands, combination bands, and overtones can interfere: they usually lead, of course, to weak intensity bands.

How varied the information in the FIR region can be, even for purely organic molecules (only light bonded atoms), is shown in Fig. 4, in which the FIR spectra of some alkyl acetic esters have been collected[27]. The assignment naturally requires the additional introduction of Raman spectroscopy.

Further difficulties arise when attempting to extract the maximum of information from the FIR spectrum in the region around and below 100 cm^{-1}. The reasons for this are as follows:

- "Hot bands" of considerable intensity occur at room temperature in this region of low-frequency vibrations.

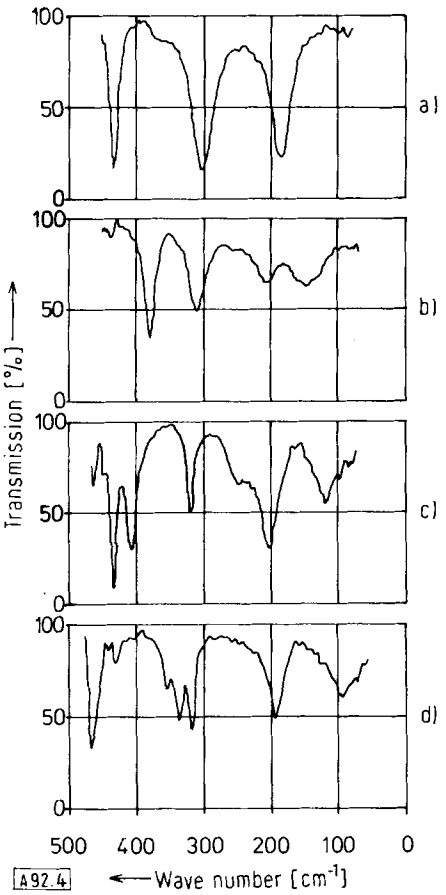

Fig. 4. FIR spectra of alkyl esters of acetic acid, CH_3COOR (dissolved in C_6H_{12}, $c \approx 5$ to 10 mol-%; layer thickness 2 mm): a) $R = CH_3$, b) $R = C_2H_5$, c) $R = i\text{-}C_3H_7$, d) $R = t\text{-}C_4H_9$.

- Low-frequency intramolecular vibrations are strongly influenced by intermolecular interactions.
- The low-frequency vibrations corresponding to the intermolecular interactions in solid and—particularly—liquid phases are usually characterized by a large variety of different force constants.

As a result, a single broad absorption band is found below 100 cm^{-1} for many substances, particularly in the liquid phase (cf. Fig. 3). The information content of this band can possibly be made accessible to the chemist by the matrix isolation technique[83]. This opens up a broad and very interesting field of application for FIR Fourier spectroscopy where, however, because of fundamental difficulties (high radiated power on cooled sample!), the Raman spectrum is no longer expected to have its usual importance as a supplementary source of information.

The assignment of an FIR spectrum is only possible when the sample to be examined has been suitably prepared. For the problems arising in this connection and their solution the reader is referred to the literature[63, 73–82].

4. Principles of the Fourier Method

4.1. The General Problem in Optical Spectroscopy

The general problem in optical spectroscopy, irrespective of the spectral region, is to determine the intensity I of electromagnetic radiation as a function of the frequency ν, the wave number $\tilde{\nu}$ or the wavelength λ. The fact that especially in

IR spectroscopy the transmittance $T_{(\tilde{\nu})} = I_{(\tilde{\nu})}/I_{0(\tilde{\nu})}$, or its negative common logarithm, the absorbance, is used, is of secondary importance and arises because a substance-specific datum is called for that must be independent of the apparatus-specific intensity distribution $I_{0(\tilde{\nu})}$. For the determination of an intensity distribution the series of waves with different wave numbers contained in a polychromatic light wave must be separated from one another in some way[42]. For this purpose a code is needed in which, in accord with information theory[43], a set of values of some measurable quantity A_i is assigned to the set of values of the wave number $\tilde{\nu}_i$:

$$(\tilde{\nu}_i) \Leftrightarrow (A_i) \tag{5}$$

Thus the intensity is measured as a function of this measurable quantity A_i, and the dependence $I_{(\tilde{\nu}_i)}$ is finally determined on decoding.

When choosing the code [Eq. (5)], the properties of electromagnetic radiation must be taken into account. For an unambiguous description of a nonpolarized, monochromatic, electromagnetic wave in a vacuum four quantities are available:

Intensity I
Wave number $\tilde{\nu}$
Direction of propagation $\vec{c}$
Phase state φ

I is one measurable quantity of interest here, and $\tilde{\nu}$ is the other. There are thus two determinable quantities still free that can be used for coding, namely $\vec{c}$ and φ.

$$(\tilde{\nu}_i) \Leftrightarrow (\vec{c}_i) \tag{5a}$$

$$(\tilde{\nu}_i) \Leftrightarrow (\varphi_i) \tag{5b}$$

The problem of coding solves itself if an apparatus is available for use as a light source by means of which monochromatic radiation of variable wave number can be produced. The wave number $\tilde{\nu}_i$ can then always be related to a specific setting X_i of one parameter of the apparatus:

$$(\tilde{\nu}_i) \Leftrightarrow (X_i) \tag{5c}$$

The decision for or against one or the other form of coding depends on the following criteria:

- Unambiguity;
- Accuracy;
- The apparatus required;
- The radiation flux through the measuring equipment.

The far infrared lies between the microwave region ($< 10\,cm^{-1}$) and the mid IR region ($> 500\,cm^{-1}$). The question is whether the methods of coding customary in these last two spectral regions and of long-proved value are applicable and useful in the FIR region.

The microwave region is a domain of nondispersive spectroscopy. Electronically controllable high-frequency tubes are used, *e.g.* reflex klystrons, which act as sources of monochromatic light.

For the medium IR region the so-called conventional dispersive spectroscopy is used. By means of a monochromator each wave train is assigned a specific propagation direction $\vec{c}_i$ corresponding to its wave number $\tilde{\nu}_i$. In practice, we use for this purpose:

- the wave-number dependence of the angle of refraction of light in a suitable prism or
- the wave-number dependence of the angle of diffraction of light by a suitable grating

At a specific distance from the dispersive element (prism or grating) one can thus, given suitable imaging optics, measure the intensity $I_{(\vec{c}_i)}$ corresponding to each direction of propagation by means of an aperture diaphragm and, behind it, a detector. The intensity distribution $I_{(\tilde{\nu}_i)}$ is then obtained by means of the well-known code (5a). Assessed by the previously mentioned criteria, this method of coding is satisfactory except in one respect: the radiation flux from the light source to the detector is considerably reduced. There are two reasons for this reduction:

- To a first approximation, the aperture diaphragm in front of the radiation detector allows the passage only of light with a specific propagation direction and thus with a specific wave number $\tilde{\nu}_i$. All light waves with $\tilde{\nu} \neq \tilde{\nu}_i$ are kept away from the detector.

  Deflection of the light at the dispersive element occurs in one dimension; accordingly, the diaphragm aperture delimiting the radiation flux muxt be a slit. The finer the details of the intensity distribution $I_{(\tilde{\nu})}$ that are to be recorded, the smaller must be the slit width. The radiation flux is thus reduced in comparison with that from a comparable circular aperture (see Section 4.2). A circular aperture can always be used if the code (5a) is not required, *i.e.* if the wave trains of differing wave numbers all have the same direction of propagation.

So long as both intense light sources and sensitive detectors are available for the spectral region under study, the reduction of the light flux is really disadvantageous (that is the signal-to-noise ratio is unfavorable and/or the time of the measurement is prolonged) only in exceptional circumstances. These exceptions occur:

- when there is a strong background absorption (*e.g.* by the solvent),
- in investigations involving high-resolution conditions, and
- in the investigation of microsamples.

Spectral regions, in which the conventional dispersive method, *i.e.* code (5a), leads in most cases to useful results, are the near-IR and the UV/VIS as well as the mid IR.

4.2. Principle of the Fourier Method Regarding Its Use in FIR Spectroscopy

The nondispersive spectroscopy practised in the microwave region is not applicable to the FIR region; electronically controllable high-frequency tubes are available only up to a maximum of a few 100 GHz (100 GHz $\hat{=}$ 3.3 cm^{-1}). It can be expected, however, that in a few years controllable lasers in the FIR region will take over the function of electronically controllable high-frequency tubes in the microwave region.—If conventional dispersive spectroscopy is introduced in the FIR region [coding according to relation (5a)], the reduced radiation flux is disadvantageous even under normal conditions, since only light sources of relatively weak intensity and relatively insensitive radiation detectors are available for the spectral region below $500\,cm^{-1}$.

For the FIR region we thus need a different kind of coding[45, 46]. This is provided by relation (5b), in which a specific phase or phase difference is unambiguously assigned to each wave number while, however, all the wave trains of different

wave number retain the same direction of propagation. The concept of phase difference makes it immediately clear that there must be two waves between which the phase difference exists. Hence the light wave to be investigated must be divided into two partial waves. Let us first assume—for the sake of simplicity—that a monochromatic plane light wave is present and that it has been divided into two partial waves of the same intensity $I_{(\tilde{\nu})}$, same direction of propagation, and same state of polarization. After we have produced a variable phase difference φ between them, we now make these partial waves overlap. The φ-dependent intensity is then measured in the overlap region:

$$I_{(\varphi)}=2I_{(\tilde{\nu})}(1+\cos\varphi) \tag{6}$$

If $\varphi=0$ or an integral multiple of 2π, then $I_{(\varphi)}$ assumes its maximum value of $4I_{(\tilde{\nu})}$. If φ is an odd multiple of π, then $I_{(\varphi)}$ has the lowest possible value, namely zero. $I_{(\varphi)}$ is called the interferogram, and the φ-dependent component in formula (6) is called the interferogram function:

$$F_{(\varphi)}=I_{(\varphi)}-2I_{(\tilde{\nu})}=2I_{(\tilde{\nu})}\cos\varphi \tag{7}$$

For the production of the variable phase difference between the two planar light waves the latter are allowed to traverse different but well-defined paths. The phase difference φ depends on the optical path difference x and on the wavelength λ or wave number $\tilde{\nu}$:

$$\varphi_{(x)}=2\pi\frac{x}{\lambda}=2\pi\tilde{\nu}x \tag{8}$$

Thus, the desired coding is achieved: according to Eq. (8), the wave number $\tilde{\nu}$ is unambiguously assigned a phase difference φ as a function of the optical path difference x. In the present experiment there is thus, according to Eqs. (7) and (8), for the monochromatic light wave under study, a corresponding experimentally measurable harmonic function—the interferogram function $F_{(x)}$—whose amplitude is proportional to the desired quantity $I_{(\tilde{\nu})}$ and whose argument is equal to the phase difference $\varphi_{(x)}=2\pi\tilde{\nu}x$:

$$F_{(x)}=2I_{(\tilde{\nu})}\cos 2\pi\tilde{\nu}x \tag{7a}$$

If, in place of monochromatic light, we are dealing with polychromatic light having any desired continuous intensity distribution, the interferogram functions corresponding to the individual wave numbers overlap without distortion with a fixed phase relationship, given by Eq. (8), between them. For an optical path difference $x=0$ all the wave trains, irrespective of the wave number $\tilde{\nu}$, give an interference maximum. Mathematically speaking, the overlap of the interferogram functions corresponding to the different wave numbers implies integration of the "monochromatic interferogram function" (7a) over all possible values of $\tilde{\nu}$:

$$F_{(x)}=2\int_0^\infty I_{(\tilde{\nu})}\cos 2\pi\tilde{\nu}x\,d\tilde{\nu} \tag{9}$$

Here $I_{(\tilde{\nu})}$ has the meaning of an intensity density, *i.e.* exactly the quantity that one wishes to determine in spectroscopic investigations. In Fig. 5 the interferogram functions for polychromatic light having a continuous intensity distribution and for monochromatic light are placed side by side. It will be seen that in the former case the amplitudes become smaller and smaller with increasing absolute value of the path difference x and finally reach zero; the cause of this is explained in Section 4.3.

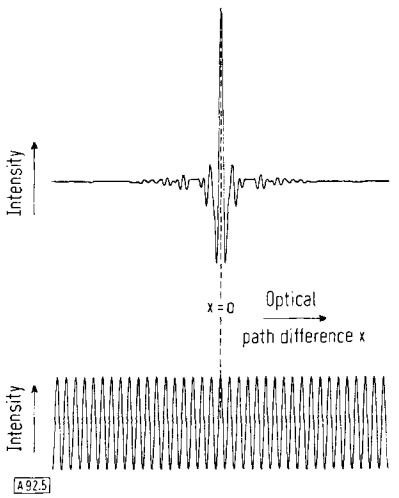

Fig. 5. Interferogram functions (sections) for polychromatic light having a continuous intensity distribution (above) and for strictly monochromatic light (below); the ordinate scales are not all the same.

After its experimental determination, the "polychromatic interferogram function" [Eq. (9)] must be investigated for its harmonic components (characterized by the wave number $\tilde{\nu}$) whose amplitudes all afford the desired value $I_{(\tilde{\nu})}$. The procedure that makes this possible is none other than a mathematical filtering of the function F based on the property of orthogonality of harmonic functions (cf. standard works on higher mathematics):

$$I_{(\tilde{\nu})}=2\int_0^\infty F_{(x)}\cos 2\pi\tilde{\nu}x\,dx \tag{10}$$

The method outlined here for investigating an intensity distribution $I_{(\tilde{\nu})}$ thus differs in fundamentals from conventional dispersive spectroscopy only in that the optical filtering of the polychromatic light wave (in the monochromator) has been replaced by mathematical filtering of the "polychromatic interferogram function" provided by the interference experiment.

Independently of whether the filtering is carried out by the optical or the mathematical method, we are always dealing with a Fourier analysis. The method in which the filtering is mathematical is called Fourier spectroscopy or Fourier transformation spectroscopy (FTS), because here, in the determination of an intensity distribution, the procedure of Fourier analysis or Fourier transformation clearly emerges in its own right.—In both methods interference experiments are carried out (in dispersive spectroscopy with multibeam interference, in Fourier spectroscopy with two-beam interference). In both methods the desired intensity distribution is provided by evaluating the interference pattern. Both methods require Fourier analysis; in conventional dispersive spectroscopy this procedure is effected by the analog monochromator/detector system, in Fourier spectroscopy by a digital or analog computer after or during the recording of the experimental quantities by

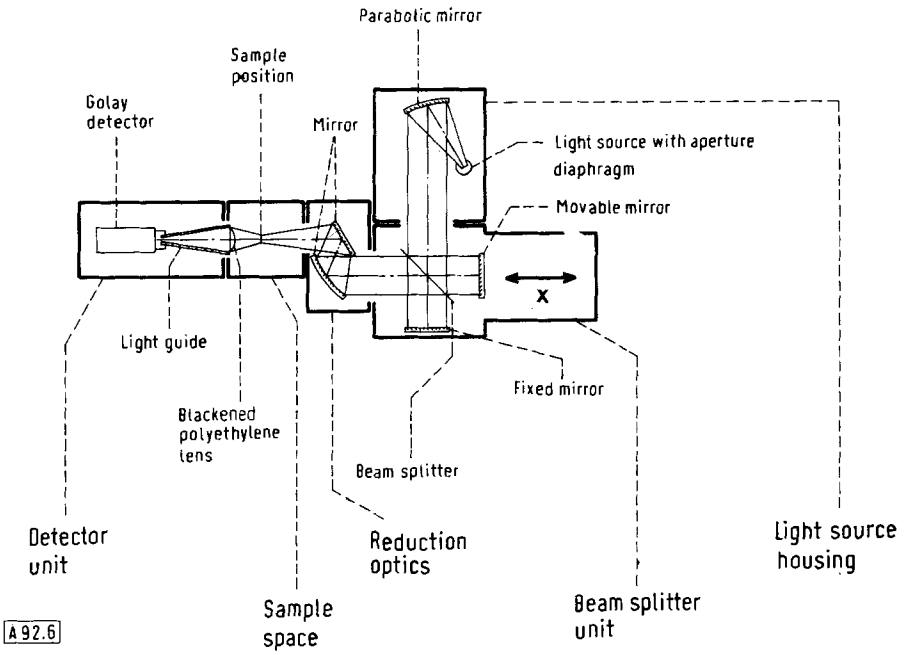

Fig. 6. Construction and optical path of a Michelson interferometer for spectroscopy in the FIR region.

the detector. The physical and mathematical bases of the Fourier method have been clearly described by, *inter alia*, *Genzel*, *Geick*, *Hurley*, *Grosse*, and *Horlick*[44, 47-51]. Specific aspects of Fourier spectroscopy are dealt with in the proceedings of the "Aspen International Conference on Fourier Spectroscopy 1970"[52].

What, then, are the advantages of the Fourier method over the conventional dispersive method?

- In the first place, all wave trains with their different wave numbers reach the detector simultaneously and not in succession. This difference in comparison with conventional dispersive spectroscopy is called "the multiplex advantage" ("Fellgett advantage").
- Secondly, there is no need for the diaphragm aperture to be in the form of a slit, since all the wave trains with their different wave numbers have the same propagation direction. With a circular aperture a radiation flux at least two orders of magnitude higher than with a slit aperture can be achieved for optical systems having the same resolving power (cf. Section 4.3) and the same collimator parameters (focal length, aperture)[4, 44]. In this connection one speaks of "throughput advantage" ("Jacquinot advantage", "étendue advantage", "aperture advantage"). The throughput advantage is naturally partly or wholly lost as soon as—*e.g.* in the investigation of microsamples—the preset aperture of the apparatus is reduced.

Only through the Fourier method has FIR spectroscopy attained its present importance in chemistry for structural determinations. Besides the above-mentioned advantages over the conventional dispersive method, it should be noted that the problems of optical filtering are more easily solved and especially that the optical systems are comparatively simpler (Fig. 6). In this respect the Fourier method is also superior to Hadamard transformation spectroscopy[42, 45, 46, 53] which otherwise is, or at least could be, of equal value. It remains, however, to explain why the Fourier method is not also generally used for the IR and UV/VIS regions.

An important reason for this—among others[44]—is the existence of problems with precision, which are not very important between 20 and 1000 μm (the FIR region) but become greater with decreasing wavelength; the shorter the wavelength of the light under study, the greater is the precision needed so as not to exceed a definite relative limit of error in the determination of the abscissa values for $F_{(x)}$ [see Eq. (9)]. It follows that even in the mid IR region (between 2.5 and 20 μm) very much greater technical effort must be expended[54] to obtain the full advantage of the Fourier method over the conventional dispersive method.

The important components of a Fourier spectrophotometer are the interferometer, which produces the experimental function $I_{(\varphi)}$ or $I_{(x)}$, and the system for evaluating the interferogram data. It is not the purpose of this review to go into details of apparatus[6, 56-62, 64] (see also Refs. [2—4]) or questions of evaluating the interferogram (Fourier transformation)[57, 65-69, 72]; here we shall only relate the theory discussed in this section to practice.

Figure 6 shows schematically the construction of an interferometer used for FIR spectroscopy (Beckman IR-720) and the optical path of the radiation. It functions on the Michelson principle. The two partial waves with the properties described above are produced by splitting the wave amplitude of a plane light wave in the beam splitter unit—this is the only component of the interferometer that is important for the explanation of the principle outlined above. (It can naturally also be the wave front that is split, as occurs in the lamellar grating interferometer[60-62].) The beam splitter itself is a film that absorbs as weakly as possible in the spectral region of interest and which permits part of the incident light to pass through while reflecting the remaining part. The light transmitted through the beam splitter falls on a fixed plane mirror parallel to the wave front. The light reflected from the beam splitter falls on another plane mirror, also parallel to the relevant wave front. Unlike the first mirror, however, the second mirror is movable in the direction normal to the wave front of the beam incident upon it, and its position determines the phase difference between the beams transmitted and reflected at the beam splitter. After respectively reflection and transmission through the splitter the two partial beams

finally reach a region (to the left of the splitter in Fig. 6) where they can overlap (see Section 4.3). Their intensities are exactly the same, since, given ideal mirrors and optimal adjustment, they have the same history. In the region where the two partial beams overlap the resulting intensity can be measured and related to the position of the movable mirror, *i. e.* the interferogram $I_{(x)}$ can be measured. Thence the interferogram function $F_{(x)}$ is obtained by simply subtracting a constant value (which is equal to the integral intensity of the two partial beams), and finally the spectrum $I_{(\tilde{\nu})}$ by subsequent mathematical filtration (Fourier transformation) of $F_{(x)}$.

All other commercially available FIR Fourier apparatus (Polytec Model FIR-30, Digilab/Cambridge Instruments Models FTS-16 and FTS-18, Bruker-Physik Model IFS-114, Coderg Model FS-4000, and Grubb Parsons Models IS-3 and Mark II)—in one or other variant—also function on the Michelson principle.

4.3. The Resolving Power of the Fourier Method

The resolving power A obtainable by means of a grating can be calculated from the expression:

$$A = \frac{\tilde{\nu}}{\Delta\tilde{\nu}} = nN \tag{11}$$

where $\Delta\tilde{\nu}$ is the distance (measured in cm^{-1}) between two infinitely sharp neighboring spectral lines that are just resolved, $\tilde{\nu}$ is the mean wave number for these two lines, N is the number of lines of the grating, and n is the grating order.

$$A = \frac{\tilde{\nu}}{\Delta\tilde{\nu}} = 2n \tag{11a}$$

Such a grating produces very broad interference maxima. This means that generally speaking a very large number of diffraction maxima must be passed through before the first occasion is encountered where the maximum for one spectral line coincides with the minimum of the other, which is the prerequisite for the fact that the existence of two adjacent spectral lines is at all observed in this experiment. As implied in Eq. (11a), the grating order n must be the higher, *i.e.* the optical path difference $n\cdot\lambda$ between the two interfering beams must be larger, the closer together are the two spectral lines, *i. e.* the smaller is $\Delta\tilde{\nu}$.

This result can be applied to the Fourier method: in place of $n\cdot\lambda$ we set the maximal optical path difference x_{max} between the two light waves that are made to overlap:

$$A = \frac{\tilde{\nu}}{\Delta\tilde{\nu}} = 2n = \frac{2n\lambda}{\lambda} = 2\tilde{\nu}x_{max} \tag{11b}$$

In order that two infinitely sharp spectral lines separated by $\Delta\tilde{\nu}$ can just be resolved, x_{max} must have the value prescribed by Eq. (11c):

$$x_{max} = \frac{1}{2\Delta\tilde{\nu}} \tag{11c}$$

$\Delta\tilde{\nu}$ can of course also be regarded as the experimental broadening, depending on the value of x_{max}, of an infinitely sharp spectral line. This is the quantity that in conventional dispersive spectroscopy is usually given as the "spectral slit width".

In practice the spectral lines are never infinitely sharp, a fact that is connected with the finite breadth of the energy levels between which the light emission processes take place.

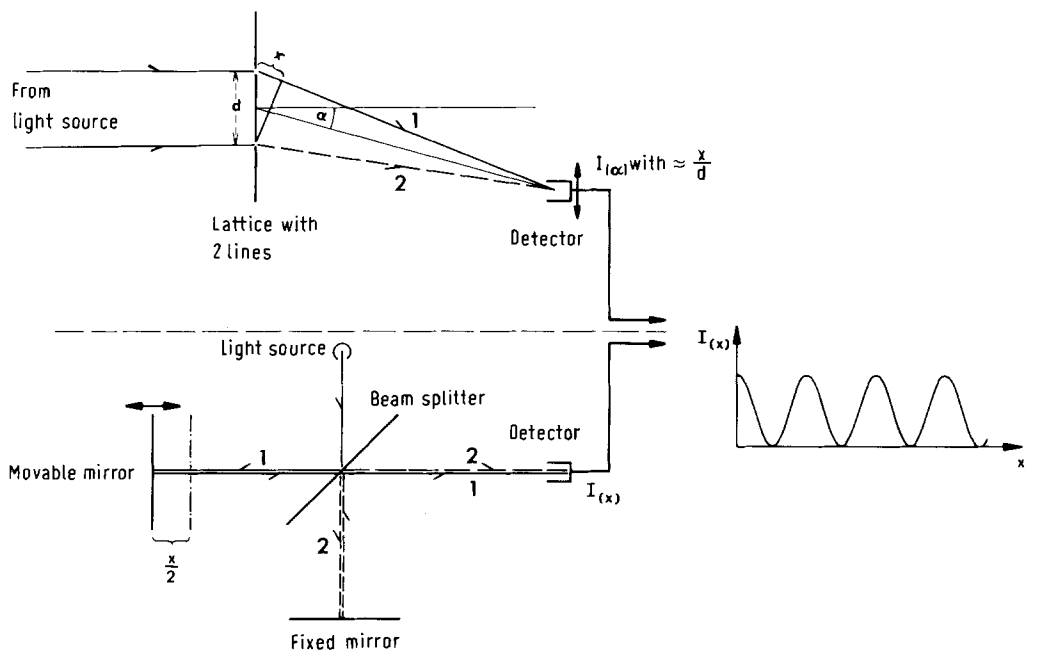

Fig. 7. Schematic representation of the phenomenon of two-beam interference on a grating with two lines (above) and in the Michelson interferometer (below). On the right is sketched the interferogram produced in both cases for strictly monochromatic light.

In the Fourier method a two-beam experiment (cf. Fig. 7: beams 1 and 2) is carried out. So far as the resolving power is concerned this amounts to a diffraction experiment with a grating (Fig. 7) containing only two lines ($N=2$); in this case we have:

The question arises how the finite breadth of the spectral lines is expressed in the interferogram function. For this purpose the Heisenberg uncertainty principle provides an answer:

$$\Delta p \cdot \Delta q \approx \frac{h}{2\pi} \tag{12}$$

where Δp is the uncertainty in momentum and Δq the uncertainty in the position of a particle (*e.g.* a photon) and h is Planck's constant. Taking into account that

$$\Delta p = \Delta\left(\frac{h}{2\pi\lambda}\right) \approx \frac{h}{2\pi}\Delta\tilde{\nu}_{1/2}$$

where $\Delta\tilde{\nu}_{1/2}$ represents the half-width of the emission lines studied, it follows from relation (12) that:

$$\Delta\tilde{\nu}_{1/2} \cdot \Delta q \approx 1$$

For photons we can replace Δq by the length of the wave train under consideration, namely the coherence length l. It follows that

$$l \approx \frac{1}{\Delta\tilde{\nu}_{1/2}} \tag{13}$$

The coherence length of a light wave is the greater, the smaller the half-width of the sharpest of the spectral lines corresponding to the light wave.

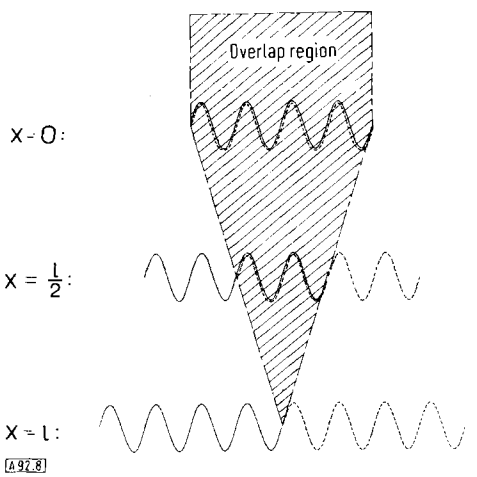

Fig. 8. Schematic representation of the overlap region between two wave trains of coherence length l in dependence on the optical path difference x.

The two partial waves produced from the light wave to be studied (cf. Section 4.2) can only interfere if they overlap completely or partially. Complete overlap occurs (see Fig. 8) when the optical path difference x is zero. The larger is x, the smaller the overlap region becomes and the less marked are the interference phenomena. Accordingly, the modulation amplitude of the interferogram function decreases continually with increasing optical path difference (Fig. 5, upper part), until it becomes zero as soon as the optical path difference equals or exceeds the coherence length ($x \geq l$). In the region where $x \geq l$, the interferogram assumes a constant value which is independent of the optical path difference and corresponds to exactly half of the maximal possible interferogram value (at $x = 0$). The continuous decrease in the interferogram function, which originates in the limited coherence length of the light wave, is called the "self-apodization"[71].

So far only more or less sharp emission lines have been discussed. In vibrational spectroscopy, however, one has to do mostly with continuous emissions weakened by absorption in specific areas. What, then, is the value of the coherence length l for such an intensity distribution, absorption occurring only within a specific spectral interval of width $2\Delta\tilde{\nu}_{1/2}$ (Fig. 9, top) and there has the form prescribed by the transmittance $T_{(\tilde{\nu})}$? The coherence length can be determined by carrying out the interference experiment described in Section 4.2 and thus measuring the region in which the interferogram function depends on the optical path difference.

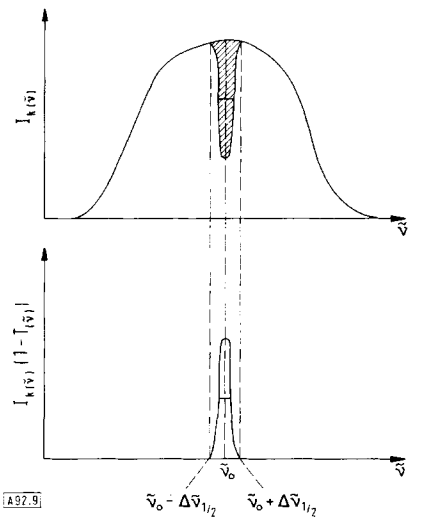

Fig. 9. Determination of the coherence length of light corresponding to a continuous intensity distribution weakened in a narrow spectral interval $2\Delta\tilde{\nu}_{1/2}$ (for explanation see text).

The interferogram function for the intensity distribution discussed here has the following mathematical form [see also Fig. 9 and Eq. (9)]:

$$F_{(x)} = 2\int_0^{\tilde{\nu}_0-\Delta\tilde{\nu}_{1/2}} I_{k(\tilde{\nu})}\cos 2\pi\tilde{\nu}x\,d\tilde{\nu} + 2\int_{\tilde{\nu}_0-\Delta\tilde{\nu}_{1/2}}^{\tilde{\nu}_0+\Delta\tilde{\nu}_{1/2}} I_{k(\tilde{\nu})}T_{(\tilde{\nu})}\cos 2\pi\tilde{\nu}x\,d\tilde{\nu} + 2\int_{\tilde{\nu}_0+\Delta\tilde{\nu}_{1/2}}^{\infty} I_{k(\tilde{\nu})}\cos 2\pi\tilde{\nu}x\,d\tilde{\nu}$$

The subscript k refers to the unweakened continuous intensity distribution.

This equation can be rearranged to:

$$F_{(x)} = 2\int_0^{\infty} I_{k(\tilde{\nu})}\cos 2\pi\tilde{\nu}x\,d\tilde{\nu} - 2\int_{\tilde{\nu}_0-\Delta\tilde{\nu}_{1/2}}^{\tilde{\nu}_0+\Delta\tilde{\nu}_{1/2}} I_{k(\tilde{\nu})}\cos 2\pi\tilde{\nu}x\,d\tilde{\nu} + 2\int_{\tilde{\nu}_0-\Delta\tilde{\nu}_{1/2}}^{\tilde{\nu}_0+\Delta\tilde{\nu}_{1/2}} I_{k(\tilde{\nu})}T_{(\tilde{\nu})}\cos 2\pi\tilde{\nu}x\,d\tilde{\nu}$$

$$F_{(x)} = 2\int_0^{\infty} I_{k(\tilde{\nu})}\cos 2\pi\tilde{\nu}x\,d\tilde{\nu} - 2\int_{\tilde{\nu}_0-\Delta\tilde{\nu}_{1/2}}^{\tilde{\nu}_0+\Delta\tilde{\nu}_{1/2}} I_{k(\tilde{\nu})}(1-T_{(\tilde{\nu})})\cos 2\pi\tilde{\nu}x\,d\tilde{\nu}$$

with

$$2\int_0^{\infty} I_{k(\tilde{\nu})}\cos 2\pi\tilde{\nu}x\,d\tilde{\nu} = F_{k(x)}$$

and

$$2\int_{\tilde{\nu}_0-\Delta\tilde{\nu}_{1/2}}^{\tilde{\nu}_0+\Delta\tilde{\nu}_{1/2}} I_{k(\tilde{\nu})}(1-T_{(\tilde{\nu})})\cos 2\pi\tilde{\nu}x\,d\tilde{\nu} = F_{\Delta\tilde{\nu}_{1/2}(x)}$$

we obtain

$$F_{(x)} = F_{k(x)} - F_{\Delta\tilde{\nu}_{1/2}(x)} \tag{14}$$

The interferogram function $F_{(x)}$ thus has two additive components:

- the contribution $F_{k(x)}$, which corresponds to the broad-band continuous intensity distribution (Fig. 9, upper part) and which decreases "rapidly" to zero (Fig. 5, upper part), and
- the contribution $-F_{\Delta\tilde{\nu}_{1/2}(x)}$, which, except for the minus sign, corresponds to an emission band with the intensity distribution $I_{k(\tilde{\nu})}(1-T_{(\tilde{\nu})})$ and half-width $\Delta\tilde{\nu}_{1/2}$ (Fig. 9, lower part) and which decreases to zero the more "slowly", the smaller is $\Delta\tilde{\nu}_{1/2}$ (half-width of the absorption band).

The coherence length l of a light wave that corresponds to a continuous intensity distribution weakened in the interval $2\Delta\tilde{\nu}_{1/2}$ by absorption (Fig. 9, upper part) can thus be estimated [Eq. (13)] if an indication of the half-width of the sharpest absorption bands to be expected is available. For solid, liquid, or dissolved samples under normal conditions, experience shows that the half-width achieved is less than $10\,cm^{-1}$ only in exceptional cases. With this standard factor Eq. (13) leads to a value of *ca.* 1 mm for the coherence length. If the maximal optical path difference is chosen as $x_{max}=2$ mm, then the total region $0\leqslant x\leqslant l$ in which the interferogram function depends on the optical path difference is usually covered. If $x_{max}<l$, then, as when the spectral slit width in conventional dispersive apparatus is made too large, experimental broadening of the absorption lines is observed, as well as disturbing artefacts—though the latter can be reduced mathematically (by apodization)[47, 70]. If $x_{max}>l$, then the measurement time is increased without any gain in spectral information, and in the region $l<x<x_{max}$ additional noise is recorded which contributes through the Fourier transformation to a worsening of the signal-to-noise ratio throughout the entire spectrum.

4.4. Spectral Region for Measurement by the Fourier Method

The spectral region usable for measurements is determined, as in every spectroscopic method, by the characteristics of the radiation from the light source, the sensitivity characteristics of the detector, and the type and efficiency of the optical apparatus. A further aspect, however, also plays an important part in the Fourier method.

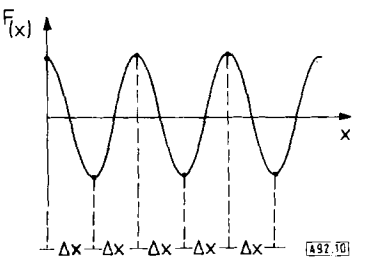

Fig. 10. Determination of the sampling intervals (for explanation see text).

In order to be able to calculate $I_{(\nu)}$ from $F_{(\tilde{x})}$ by Eq. (10) one must care for numerical acquisition of $F_{(x)}$ between $x=0$ and $x=x_{max}$, which is not possible continuously but only at specific intervals Δx (Fig. 10). This procedure in which Eq. (15) is used with $m=0,1,2\ldots$

$$x=m\cdot\Delta x \tag{15}$$

is called digitization of the function $F_{(x)}$, Δx the sampling interval[55]. Due to the digitization of the interferogram function it is, of course, necessary to convert the integral in Eq. (10) into a sum. After the choice of Δx the upper limit of the spectral region to be measured is already fixed because, according to the sampling theorem of information theory, harmonic functions can be characterized unambiguously in digital form only when at least one ordinate value per half-period is sampled. The Fourier transformation of $F_{(x)}$ can thus be effected unambiguously only if this condition is fulfilled for all harmonic functions making up $F_{(x)}$. Since, however, the periods of these harmonic functions are exactly equal to the wavelengths of the polychromatic light studied, only light of wavelength $\lambda>\lambda_{min}$ may contribute to the measured signal $I_{(x)}$; we have:

$$\lambda_{min}=2\Delta x=\frac{1}{\tilde{\nu}_{max}}$$

or

$$\tilde{\nu}_{max}=\frac{1}{2\Delta x} \tag{16}$$

Wave trains with $\tilde{\nu}>\tilde{\nu}_{max}$ contribute intensity to the wave trains with $\tilde{\nu}<\tilde{\nu}_{max}$; this means that the form of coding [relation (5b)] is not unambiguous. Unambiguity can, however, be brought about if all the intensity contributions with wave numbers $\tilde{\nu}>\tilde{\nu}_{max}$ are eliminated by optical or electrical filtering.

The contributions with wave numbers $\tilde{\nu}_2>\tilde{\nu}_{max}$ to the intensity expected at wave numbers $\tilde{\nu}_1<\tilde{\nu}_{max}$ can be determined as follows: The "monochromatic interferogram function"

$$F_{1(x)}=I\cos 2\pi\tilde{\nu}_1 x$$

is assigned to the wave number $\tilde{\nu}_1$. From this, with allowance for Eqs. (15) and (16), we obtain

$$F_{1(m)}=I\cos\frac{m\pi\tilde{\nu}_1}{\tilde{\nu}_{max}}$$

Then we determine all those "monochromatic interferogram functions"

$$F_{2(m)}=I\cos\frac{m\pi\tilde{\nu}_2}{\tilde{\nu}_{max}}$$

that with $\tilde{\nu}_2 > \tilde{\nu}_{max}$ have the same value as $F_{1(m)}$ at the same m; after digitization they can no longer be distinguished from $F_{1(m)}$. Finally, the calculation gives:

$$\tilde{\nu}_2 = \begin{cases} (2n+2)\tilde{\nu}_{max} - \tilde{\nu}_1 \\ 2n \quad \tilde{\nu}_{max} + \tilde{\nu}_1 \end{cases} \tag{17}$$

If it is not certain that all the wave trains with $\tilde{\nu} > \tilde{\nu}_{max}$ are excluded by optical or electrical filtering, then the intensity measured for $\tilde{\nu}_1 < \tilde{\nu}_{max}$ may arise wholly or partially from intensity contributions with $2\tilde{\nu}_{max} \pm \tilde{\nu}_1$, $4\tilde{\nu}_{max} \pm \tilde{\nu}_1$, ... *etc.*, the so-called false light contributions.

The problem of false light contributions arises not only for the Fourier method but also in conventional dispersive spectroscopy. Here the unambiguity of the assignment (5a) can be safeguarded only by optical filtering, which is most efficiently achieved with double or triple monochromators. The false light (also misleadingly called stray light) that has to be filtered out arises mainly from interfering grating orders.

In a search for errors not only the spectrum but also the interferogram should be thoroughly and precisely inspected. Differentiation of the various types of error (*e.g.* electronic disturbances, wrongly chosen instrumental parameters, unsuitable preparation of the sample) is often only possible by checking the interferogram alone ("Qualitative Interferogram Evaluation")[82].

Example 1

Figure 11 shows that a slightly structured, continuous intensity distribution $I_{(\tilde{\nu})}$ provides an interferogram function $F_{(x)}$ that is dependent on the optical path difference x over only a relatively narrow region (Fig. 11a). On the other hand, the optical path difference at which the interferogram function becomes constant (*e.g.* identical to zero) is the larger, the sharper are the spectral lines present in the intensity distribution $I_{(\tilde{\nu})}$ (Fig. 11b, rotational transitions of water vapor).

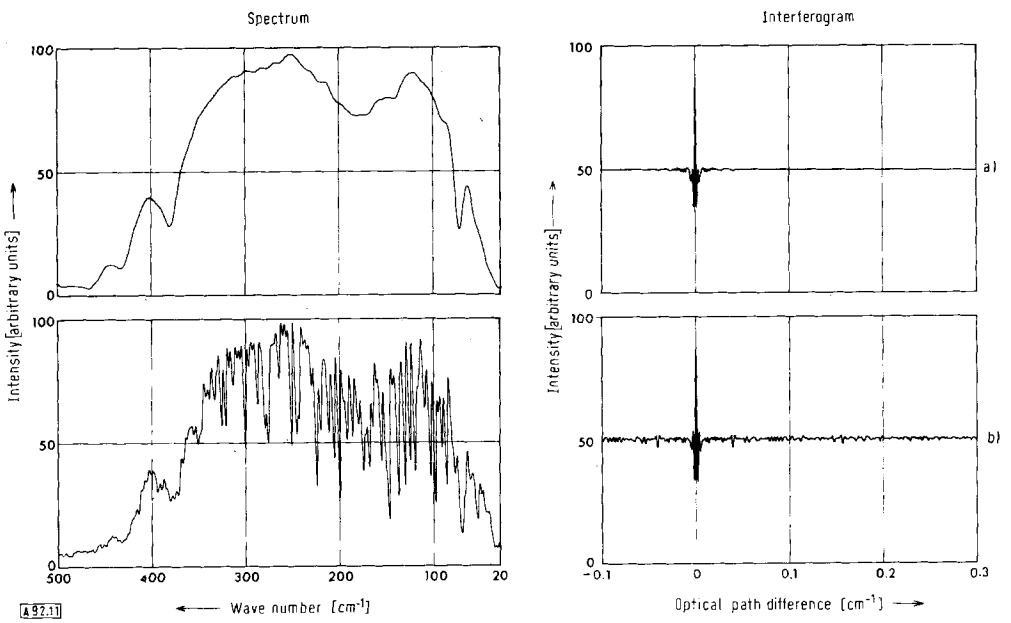

Fig. 11. Comparison of the interferogram and the spectrum in the cases of (a) continuous, and (b) discrete spectral intensity distributions.

A further contribution is provided by light that passes through the monochromator by routes deviating from the prescribed beam path.

5. Simple Examples of the Interpretation of Interferograms

To obtain a spectrum on a Fourier spectrophotometer the Fourier transformation must in principle be carried out quantitatively. This is possible only with the aid of data-processing machines, except for strictly monochromatic radiation (Fig. 5, lower part) or for polychromatic radiation that contains only a few, strictly monochromatic, components, neither of which are of practical interest. After some practice, however valuable qualitative information can be extracted from the interferogram without a quantitative Fourier transformation. The labor of qualitatively interpreting interferograms will materially assist the beginner in appreciating the principle of the Fourier method.

The explanation of this follows from the Heisenberg uncertainty principle (Section 4.3), which provides a connection between the coherence length of a light wave and the half-width of the corresponding spectral lines or bands. Thus, one can infer from the interferogram function alone whether there are more or less sharp emission or absorption areas in the intensity distribution studied.

Example 2

The periods of the harmonic functions that form the interferogram function are the larger, the longer are the wavelengths of the light studied. This can be seen in Figure 12.

The figure shows two intensity distributions—one mainly short-wave with a mean wavelength of about 26 μm (386 cm^{-1}) and a second, mainly long-wave, with a mean wavelength of about 155 μm (65 cm^{-1})—together with the corresponding interferogram functions. The ratio of the mean wavelengths is about 1:6 and the same ratio is found again in the separations of the two central minima in the corresponding interfero-

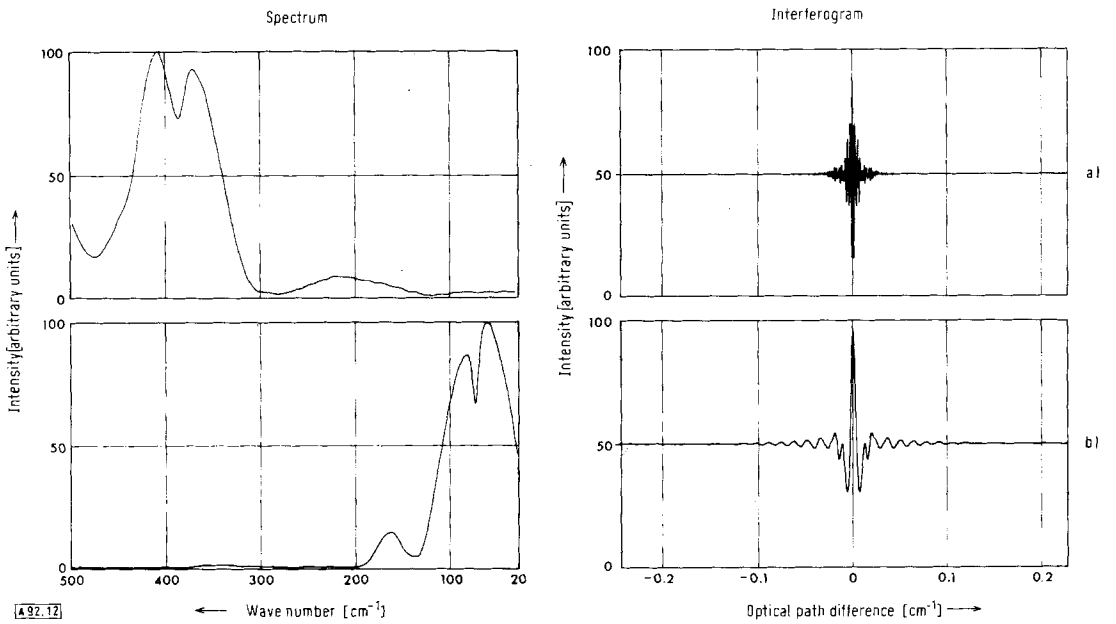

Fig. 12. Comparison of the interferogram and the spectrum for mainly shortwave (a) and mainly long-wave light (b).

gram functions. The other minima in the interferogram function corresponding to the shorter-wave radiation likewise follow one another more closely than in those corresponding to the longer-wave radiation. Thus, from the interferogram function alone one can decide whether mainly short-wave or mainly long-wave light is concerned. In this way one can *e.g.* determine whether the attempts to exclude light-scattering effects during the preparation of the sample were successful.

Example 3

Periodic interference of the FIR spectrum prejudicial to the substance-specific character of the information obtained is often observed; this can have various causes, which can be unambiguously identified from the interferogram function:

- Disturbing impulses in the interferogram function (Fig. 13a); they are caused by electrical or mechanical interferences and are not symmetrical about the position $x=0$.
- Internal reflection in a plane-parallel layer (*e.g.* in the cell, in the sample carrier, or in the sample itself[81,82]); figure 13b illustrates this case: the spectral intensity distribution corresponds to the apparatus characteristic of a Michelson interferometer where a plane-parallel almost absorption-free paraffin wax film about 100 µm thick has been introduced into the path of the beam. The internal reflection in a single plane-parallel layer produces in the interferogram two side-burst peaks arranged symmetrically around $x=0$ (arrows in Fig. 13b). They are converted by the Fourier transformation into the periodic interference observed in the spectrum ("channel spectra"). If we use for the Fourier transformation only that part of the interferogram function that lies between these two maxima, the interference in the spectrum disappears; admittedly, in certain circumstances the resolving power is then too small for the determination of the true band form (see Section 4.3; cf. Fig. 13b and 13c, absorption band at 72 cm^{-1}). The plane-parallelism between the relevant surfaces must then be destroyed in some other way; in the present example this was done with the

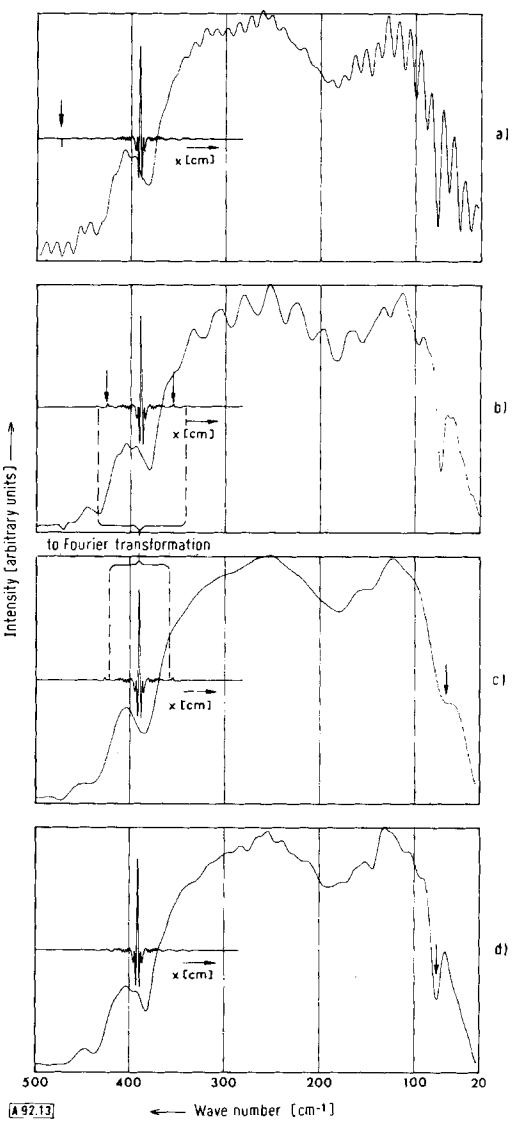

Fig. 13. Causes of periodic interference of the FIR Fourier spectrum (for explanation see text).

paraffin wax film (wedge shaped), which finally gave the interferogram and the spectrum shown in Figure 13d.

- Overlapping of a boxcar function (error in the determination of the interferogram function from the interferogram) or a triangular function (so-called drift in the interferogram) on the interferogram function used for the Fourier transformation[82].

6. Concluding Remarks

Introduction of the Fourier method into FIR spectroscopy has not only led to a considerable facilitation of work and an improvement in the quality of the spectra, but has also fostered interest in the FIR region. This is the case especially for the introduction of FIR spectroscopy into organic chemistry. Owing to the absence of heavy bonded atoms in organic molecules, the information content of the FIR spectrum was long underestimated. It followed that the demands on finance and time made by the measurement of FIR spectra by the conventional dispersive method were rightly assessed as too great. The introduction of the Fourier apparatus has certainly not eased the financial burden, or at the most slightly so in isolated cases; but its efficiency—greater than that of the conventional dispersive apparatus—has encouraged attack on, and indeed in some cases the solution of, the problems set out in Sections 2 and 3. The region below $100\,cm^{-1}$, which is especially important for the study of weak intermolecular interactions, would certainly have remained inaccessible had it not been for the Fourier apparatus, and the expansion of collections of spectra far into the FIR region[84] would presumably never have happened without the Fourier apparatus.

In recent years the Fourier method has received recognition and more extended use in NMR spectroscopy[65, 85-88], as it has in FIR spectroscopy. In particular, ^{13}C-NMR spectroscopy owes its present importance as an analytical tool exclusively to the Fourier method.

This progress report is based on five years experience in the field of FIR Fourier spectroscopy which the author collected in the Anwendungstechnik and Training Department at Beckman Instruments GmbH in München (Germany). Opportunity is taken here to express thankful recognition of the possibilities offered by the firm Beckman to carry out relevant scientific work—particularly in the field of molecular spectroscopy. Thanks are due to Prof. Dr. B. Schrader (Universität Dortmund) and Priv. Doz. Dr. P. Bleckmann (Universität Dortmund) for valuable suggestions and expert opinion on parts of the manuscript, and to Grad. Ing. K. Dabelstein (Beckmann Instruments) for help with the measurements necessary for this work.

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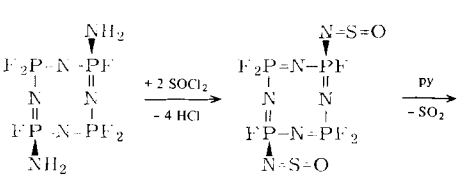
COMMUNICATIONS

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

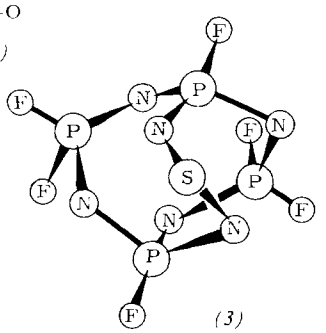
A Cyclophosphazene Spanned by a Sulfur Diimido Group[**]

By *Herbert W. Roesky* and *Enno Janssen*[*]

Although the chemistry of fluorinated cyclophosphazenes has been actively studied in recent years[1], derivatives having inorganic ring bridges have nevertheless remained unknown. Consideration of a model of $P_4N_4F_8$ revealed that a central bridge of this kind would have to have at least three members.



(1) (2)



(3)

Treatment of $P_4N_4F_6(NH_2)_2$ *(1)* with $SOCl_2$ afforded $P_4N_4F_6(NSO)_2$ *(2)*. In the presence of pyridine, *(2)* eliminates sulfur dioxide to give a low yield of 1,5,7,7,10,10-hexafluoro-3λ^4-thia-2,4,6,8,9,11-hexaaza-1λ^5,5λ^5,7λ^5,10λ^5-tetraphospha-bicyclo[3.3.3]undeca-2,3,5,7,9(1),10-hexaene *(3)*.

Compound *(3)* is a yellowish crystalline solid which sublimes at 25 °C/0.5 torr and melts at 57 °C. Its composition is proved by complete elemental analysis, and its monomeric structure in the liquid and gaseous state follows from the molecular weight (exp. 350, cryoscopic in C_6H_6) and the mass spectrum [M^+: *m/e* 354 (48 %)]. In the ^{19}F-NMR spectrum two multiplets appear in the intensity ratio of 1 : 2, their centers of gravity lying at $\delta_F = 59.8$ ppm and 66.2 ppm. The spectrum is independent of temperature, an argument strongly supporting the proposed structure *(3)*.

Procedure:

$P_4N_4F_6(NSO)_2$[2] (4.2 g, 0.01 mol) is heated in the presence of a catalytic amount of pyridine (2 drops) on a water bath for 2 d. Sublimation of the reaction product affords *(3)* (0.28 g, 8 %). This compound is also formed in low yield during the preparation of $P_4N_4F_6(NSCl_2)_2$ by heating of $P_4N_4F_6(NH_2)_2$ and sulfinyl chloride with elimination of SO_2 and HCl.

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Tellurium(IV) Iodide: Tetrameric Te_4I_{16} Molecules in the Solid[**]

By *Volker Paulat* and *Bernt Krebs*[*]

The structures of chalcogen(IV) halides investigated up to now are determined largely by the stereochemical activity of the S^{IV}, Se^{IV}, and Te^{IV} nonbonding electron pairs. Gaseous SF_4 and SeF_4 (also $TeCl_4$ in the gas phase)[1] have the monomeric C_{2v} structure predicted by the VSEPR theory[2]; in solid TeF_4, on the other hand, square-pyramidal TeF_5 groups are linked *via* corners to form chains, the localized lone pair (E) completing octahedral TeF_5E coordination[3]. The structures of solid $TeCl_4$[4], $TeBr_4$[5], and $SeCl_4$[6] contain tetrameric

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cubane-like molecules with distorted octahedral coordination around Te and Se, the lone pair being largely delocalized.

Our investigations on Te^{IV} iodide showed this compound to have a molecular structure in the solid which has not yet been observed in binary inorganic substances.

Single crystals for X-ray structure analysis were obtained by repeated sublimation at 100 °C in evacuated glass tubes of 5 cm length; the starting material was purified TeI_4, prepared by reaction of concentrated aqueous solutions of telluric acid and hydrogen iodide[7].

TeI_4 crystallizes in the orthorhombic space group Pnma with the cell constants $a = 13.635$, $b = 16.798$, $c = 14.624$ Å, $Z = 16$ TeI_4, $d_x = 5.04$, $d_{exp} = 5.02$ g/cm³ (literature values $a = 13.54$, $b = 16.73$, $c = 14.48$ Å[8]). The structure was solved from 3800 diffractometer data using Patterson methods and was refined to a conventional R factor of 5.3%.

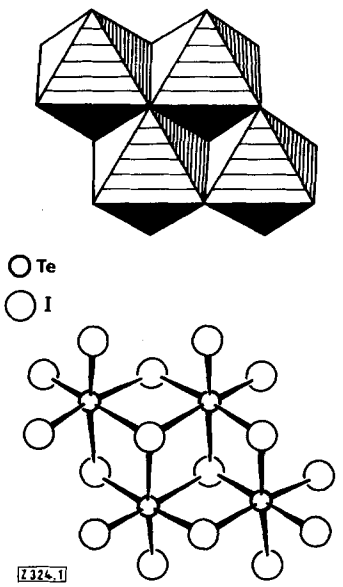

Fig. 1. Molecular structure of tellurium tetraiodide $(TeI_4)_4$ in the crystal.

The structure contains tetrameric Te_4I_{16} molecules as shown in Figure 1 which are built up of edge-sharing TeI_6 octahedra. This structural type has hitherto only been observed in titanium(IV) alkoxides[9]. The Te_4I_{16} molecule has exact C_s symmetry in the crystal, and is very close to an idealized C_{2h} symmetry. The Te—I bond lengths are: 2.752(2) to 2.788(2) Å (terminal, average 2.768 Å), 2.932(2) to 3.278(2) Å (I bonded to 2 Te, average 3.108 Å) and 3.198(3) to 3.241(2) Å (I bonded to 3 Te, average 3.227 Å). The I···I distances in the almost undistorted close packing of iodine atoms (sequence ABAC) are between 3.891(3) and 4.540(2) Å and rule out significant intermolecular bonding.

Comparison of the bond data in the homologous series TeF_4—$TeCl_4(TeBr_4)$—TeI_4 reveals an increasing delocalization of the Te^{IV} lone pair. This effect is likewise observed in compounds of other s^2 elements (Sn^{II}, Pb^{II}, As^{III}, Sb^{III}, Bi^{III}, I^V) and correlates with the gradation of electronegativities and polarizing power of the halogens.

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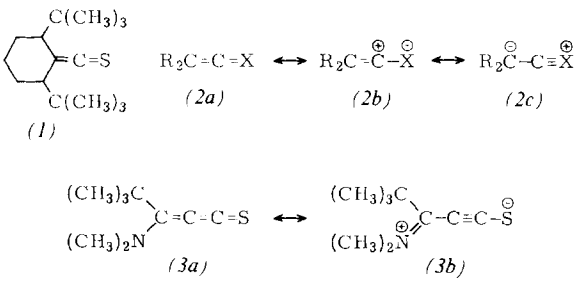
X-Ray Structure Analysis of a Dialkylthioketene

By *Ernst Schaumann*, *Surya Harto*, and *Gunadi Adiwidjaja*[*]

In contrast to the extensively studied ketenes, the thioketenes are generally very unstable. However, some representatives bearing bulky substituents can actually be isolated[1, 2]. An X-ray structure analysis performed on the crystalline thioketene *(1)* (m. p. 37 °C)[2a] should contribute to a better understanding of this class of compounds.



Compound *(1)* forms monoclinic crystals (space group $P2_1/c$; $a = 10.834$, $b = 12.251$, $c = 12.122$ Å; $\beta = 108.35°$). On the basis of 1324 significant reflections the structure was solved by direct methods and, as previously described[3], refined to an R value of 0.045.

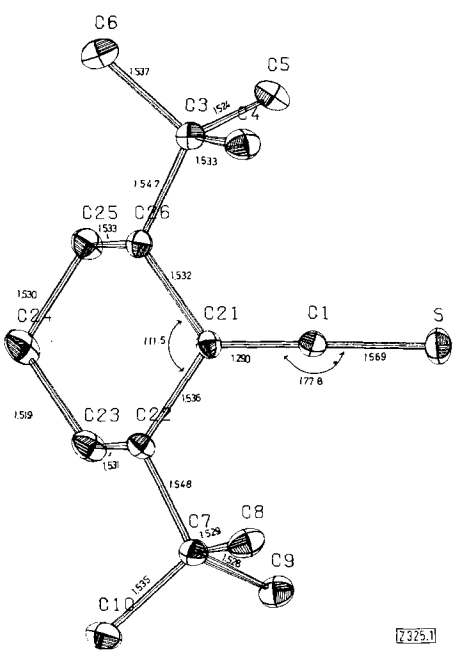


Fig. 1. Molecular structure of thioketene *(1)* with bond lengths [Å] (maximum standard deviation 0.006 Å) and important bond angles [°] (±0.3°).

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The calculated molecular structure (Fig. 1) confirms the formulation as a monomeric thioketene *(1)*. The practically linear heterocumulene system is joined to a cyclohexane ring in the chair conformation. The *tert*-butyl groups are arranged equatorially in the *gauche* conformation and screen the thioketene system, thus explaining the particular stability of *(1)* and its reluctance to undergo cycloaddition reactions[2b].

The exocyclic double bond C^1—C^{21} is markedly shorter than in ketenes (dimethylketene: $r_{C=C}=1.314$ Å)[4]; a resonance formula *(2c)* weakening the double bond, whose significance in ketenes (X=O) is confirmed by MO calculations[5a] and ^{13}C-NMR data[5b], should therefore play at least no greater role in the thioketenes (X=S) than in the ketenes themselves. In accord with the formal sp hybridization of C^1, the CS bond length in *(1)* is shorter than in thioformaldehyde ($r_{C=S}=1.611$ Å)[6], and also significantly shorter than in the alkylidenethioketene *(3)* ($r_{C=S}=1.621$ Å)[7], which indicates a considerable contribution by the acetylenethiolate resonance structure *(3b)*. On the other hand, the CS bond length in *(1)* is greater than in carbon disulfide ($r_{C=S}=1.554$ Å)[8] where a resonance structure diminishing the electron density in the CS bond, which is analogous to *(2b)*, affects two sulfur atoms and thus becomes less effective for the individual bond. Here it should be noted that the direction indicated by *(2b)* for the polarization of the CS double bond in *(1)* does not follow unequivocally from its reactions[2]. Nor does the S(2p) ESCA spectrum of *(1)*[9], which indicates relatively nonpolar sulfur at 162.7 eV, permit any such decision.

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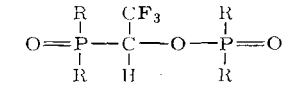
1,1-Bis(diphenylphosphoryl)-2,2,2-trifluoroethanol—A New Intermediate of Trifluoroacetyldiphenylphosphane Oxidation by Molecular Oxygen[**]

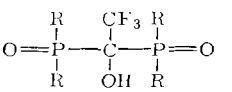
By *Ekkehard Lindner, Hans-Dieter Ebert*, and *Hans Lesiecki*[*]

Combination of (perfluoro)acyl groups with organophosphorus groups generally leads to labile, and hence highly reactive compounds of the type $(RCO)_nPR_{3-n}$[1]. If molecular oxygen is allowed to act on perfluoroacyldiarylphosphanes ($n=1$) then a complicated sequence of reactions ensues at room temperature, with participation of small amounts of H_2O, to form (1-diarylphosphoryl-1*H*-perfluoroalkyl)diarylphosphinates $(OPR_2)_2OCHR_f$, for example *(1)*, carbon dioxide, and the corresponding 1-H-perfluoroalkanes R_fH[2].



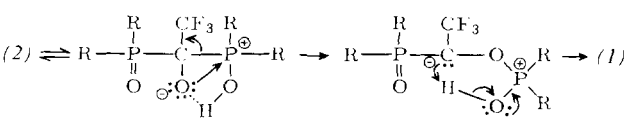
(1), R = C_6H_5

Since this kind of reaction has a considerable scope, we have attempted to gain an insight into the complicated sequence of events and have now succeeded in isolating a new intermediate: If the oxidation of trifluoroacetyldiphenylphosphane in diethyl ether is carried out in a polyethylene vessel then a colorless compound, m. p. 159—161 °C, precipitates within a few minutes, which is identified as 1,1-bis(diphenylphosphoryl)-2,2,2-trifluoroethanol *(2)* on the basis of elemental analysis, and IR and mass spectra.



(2), R = C_6H_5

The IR spectrum of *(2)* contains a broad intense band at 3080 cm^{-1} corresponding to an O—H stretching mode. This absorption is masked by a sharp minimum for the arene C—H vibrations at 3062 cm^{-1}. A band at 1350 cm^{-1} can be interpreted as an O—H deformation frequency. The alcohol *(2)* recently proposed as intermediate in the oxidation of $CF_3COP(C_6H_5)_2$[3] proves to be thermally labile and undergoes irreversible isomerization on heating in various solvents (alcohols, halogenated hydrocarbons, *etc.*) to give the more stable (1-diphenylphosphoryl-2,2,2-trifluoroethyl)diphenylphosphinate *(1)*:



In the usual glass vessels the isomerization *(2)*→*(1)* is catalyzed to such an extent that the isolation of *(2)* becomes impossible. The isomerization can be followed by IR spectroscopy: The broad O—H band disappears in favor of a sharp alkane C—H stretching absorption at 2924 cm^{-1}. The hydrogen atom in *(2)* and *(1)* comes from traces of moisture in the oxygen used and can be replaced by deuterium if the oxygen stream is moistened with D_2O after purification in a molecular sieve.

Procedure:

Through a solution of $CF_3COP(C_6H_5)_2$ (4.5 g, 16 mmol) in diethyl ether prepared in a polyethylene vessel is passed a vigorous current of oxygen. After *ca.* 10 min the alcohol *(2)* precipitates as colorless crystals. The crystals are filtered off, washed with diethyl ether, and vacuum dried. Yield 1—2 %.

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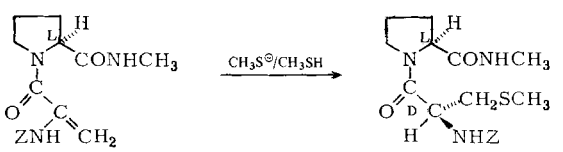
Optical Induction During Biomimetic Formation of Cysteine[**][1]

By *Ulrich Schmidt* and *Elisabeth Öhler*[*]

The peptide hormones kallidin, eledoisin, and β-melanotropin contain L-serine-L-proline segments, and L-cysteinyl-L-proline units are found in the hormones β-corticotropin releasing factor, oxytocin, isotocin, vasopressin, and vasotocin. β-Methyl-D-cysteinyl-L-proline is a component of a heterodetic cyclotetrapeptide in the antibiotics nisin and subtilin[3]. The thioether of this ring is probably formed by intramolecular addition of a mercapto group to the double bond of aminocrotonic acid in α-aminocrotyl-L-prolylglycyl-L-cysteine.

This suggests that the spatial course of addition of hydrogen sulfide or thiols to dehydroalanine—an essential reaction for cysteine biosynthesis—can be directed by an amino acid joined by a peptide-type linkage to dehydroalanine. This concept is confirmed by a simple model: *N*-benzyloxycarbonyldehydroalanyl-L-prolinemethylamide *(1)* adds methanethiol in a sodium methanethiolate-catalyzed reaction to give almost exclusively (optical yield at least 85%) *N*-benzyloxycarbonyl-*S*-methyl-D-cysteinyl-L-prolinemethylamide *(2a)*. The starting compound *(1)* was prepared according to the method of *Patchornik*[4] by reaction of *(2b)* with CH_3Br/HCOOH and degradation of the sulfonium salt in aqueous $NaHCO_3$ solution (yield 75%)[2].



(1) *(2a)*

Z = C_6H_5–CH_2–O–CO [+ 15% *(2b)*]

Compound *(2a)* and the diastereomeric L-cysteinyl derivative *(2b)* can be distinguished on the basis of the chemical shifts of the *S*-methyl and *N*-methyl protons in the NMR spectrum [*(2a)*, δ = 2.10 (s), 2.67 (d); *(2b)*, δ = 2.14 (s), 2.62 (d) (both 100 MHz, in $CDCl_3$, TMS internal standard)]. *(2b)* was obtained in 68% yield from Z-L-Cys(SMe)-OH and L-H-Pro-$NHCH_3$ by the DCC method[2], m.p. 127—130 °C (from ethyl acetate), $[\alpha]_D^{20} = -84°$ ($c = 1.096$ in $CHCl_3$).

In order to establish the configuration of *(2)* beyond doubt we prepared the enantiomer *N*-benzyloxycarbonyl-*S*-methyl-L-cysteinyl-D-prolinemethylamide *(2c)* in 64% yield from Z-L-Cys(SMe)-OH and D-H-Pro-$NHCH_3$ by the DCC method; m.p. 112—113 °C (from ethyl acetate/ether), $[\alpha]_D^{20} = +54°$ ($c = 1.094$ in $CHCl_3$). The enantiomer proved to be identical with *(2a)*, except for the opposite sign of rotation.

N-Benzyloxycarbonyl-S-methyl-D-cysteinyl-L-prolinemethylamide (2a)

A solution of $NaOC_2H_5$ (1 mmol) and methanethiol (500 mg) in anhydrous ethanol (4 ml) is added to a solution of *(1)* (330 mg, 1 mmol) in anhydrous ethanol (4 ml) and the mixture stirred for 2 h. The ethanol is then removed under vacuum, and the residue taken up in dichloromethane (20 ml) and washed twice with H_2O (2 × 3 ml). The CH_2Cl_2 solution is dried over Na_2SO_4, evaporated under vacuum, and the oily residue purified by chromatography on silica gel (eluant: chloroform/methanol 9:1). The NMR spectrum of the oil obtained in this way (in $CDCl_3$) contains signals for both *(2a)* and *(2b)* [*(2a)*:*(2b)* = 8.5:1.5]. On rubbing with ethyl acetate/ether, 290 mg of *(2a)* crystallized; m.p. 105—110 °C (from ethyl acetate/ether); $[\alpha]_D^{20} = -55°$ ($c = 0.985$ in $CHCl_3$), yield 77%.

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CAS Registry numbers:
(1), 53941-82-5; *(2a)*, 57620-58-3; *(2b)*, 57620-59-4; *(2c)*, 57620-60-7; methanethiol, 74931

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Synthesis of Phosphorus Ylides at a Cobalt-Complex Center[**]

By *Hans-Friedrich Klein* and *Reinhard Hammer*[*]

During oxidative additions to tetrakis(trimethylphosphane)-cobalt(0)[1] the electronic configuration of the metal changes from d^9 to d^8; this results in a 2:1 stoichiometry for such reactions in accordance with Eq. (1).

$$2\ L_4Co + X\text{–}Y \longrightarrow L_4CoX + L_3CoY + L \qquad (1)$$

L = $(CH_3)_3P$; X = H, Y = Cl; X = CH_3[2], Y = Br

We have found that the addition of 1,1-dihaloalkanes in the sense of Eq. (1) [*e.g.* X = RCHCl, Y = Cl] does not stop at the stage of the haloalkylcobalt(I) complex, but proceeds with 3:2 stoichiometry in accordance with Eq. (2) to give a complex cobalt dihalide having two ylidic alkylenetrimethylphosphorane ligands

$$3\ L_4Co + 2\ R^1R^2CCl_2 \xrightarrow[-10\,°C]{\text{pentane}} [(CH_3)_3PCR^1R^2]_2CoCl_2 + 2\ L_3CoCl + 4\ L \qquad (2)$$

L = $(CH_3)_3P$

(1). $R^1 = R^2 = H$: blue solid[4], 73%
(2). $R^1 = R^2 = D$: blue solid, 75%
(3). $R^1 = H$, $R^2 = CH_3$: blue crystals, 55%, sparingly soluble in THF, dec. > 108 °C
(4). $R^1 = H$, $R^2 = Si(CH_3)_3$: blue crystals, 43%, soluble in benzene and THF, dec. > 76 °C

In this reaction a *chlorine-free* carbene is formally transferred and not a chlorocarbene as in the Wittig reaction[5]. *(1)* has a magnetic moment ($\chi_g = 26.3 \times 10^{-6}$ g cm^{-3}; $\mu_{eff} = 4.3_9\ \mu_B$), which is in good agreement with that of the isoelectronic $[(CH_3)_3PO]_2CoCl_2$[6]. As shown by the IR spectrum on reaction with CD_2Cl_2 deuterium is distributed over all C atoms of *(2)*.

It seems plausible that the overall reaction proceeds in three steps:

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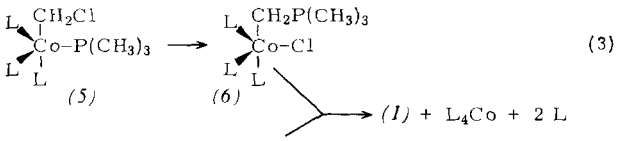
1) Oxidative addition according to Eq. (1), for example with $X=CH_2Cl$, $Y=Cl$. The hypothetical intermediate *(5)* in Eq. (3) is formulated analogously to the stable complex L_4CoCH_3[1].

2) Reaction of the carbenoid moiety $Co—CH_2—Cl$ in *(5)* according to Eq. (3) to give *(6)*. In the synthesis of *(1)* according to Eq. (2) the carbene trapping agent cyclohexene can be used as reaction medium without lowering the yield of *(1)* or norcarane being detectable by mass spectroscopy.

3) Disproportionation of the second intermediate *(6)* as already observed earlier in the reaction according to Eq. (4)[4].



(5) *(6)* *(1)* + L_4Co + 2 L (3)

$$2\ L_3CoCl + 2\ (CH_3)_3P{=}CH_2 \qquad (4)$$

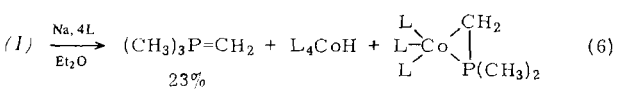
L = $(CH_3)_3P$

Since the by-product L_3CoCl [Eq. (2)] is formed as intermediate of the reduction during production of L_4Co[1], from cobalt chloride, trimethylphosphane (L) and magnesium in tetrahydrofuran (THF), it could be utilized in a simple batch synthesis of *(1)* according to Eq. (5); this affords indeed satisfactory yields:

$$CoCl_2 + 4\ L + 2\ CH_2Cl_2 + 2\ Mg \xrightarrow{THF} (1) + 2\ MgCl_2 + 2\ L \qquad (5)$$

L = $(CH_3)_3P$ 70%

The ylide ligand in *(1)* is strongly bound and is not displaced by chelating agents. It is partially liberated only by reduction with metals in presence of sufficient amounts of trimethylphosphane, but not without a further part being decomposed in some unknown way. The reduced cobalt stabilizes in the form of known trimethylphosphane complexes[4, 7].



(1) $\xrightarrow[Et_2O]{Na,\ 4L}$ $(CH_3)_3P{=}CH_2$ + L_4CoH + $L_3Co(CH_2)P(CH_3)_2$ (6)

23%

L = $(CH_3)_3P$

Procedure:

A mixture of anhydrous $CoCl_2$ (1.33 g, 10.2 mmol), $(CH_3)_3P$ (3.8 ml, 40.0 mmol) and magnesium turnings (500 mg, 20.5 mmol) in THF (30 ml) is stirred at 20 °C under protective gas (nitrogen) until the solution turns reddish brown. A solution of CH_2Cl_2 (1.31 ml), 20.4 mmol) in THF (15 ml) is then cautiously added dropwise such that the brown coloration of the solution is just sustained over the blue precipitate (towards completion the dropwise addition must be carried out very slowly). The final mixture is stirred for 2 h, filtered, and the product washed with 50 ml THF in small portions until the washings are colorless. After 3 hours' drying at 20 °C/0.1 torr, analytically pure *(1)* (2.20 g, 70 %) is obtained.

A suspension of *(1)* (2.00 g, 6.45 mmol) in ether (20 ml) is reduced with Na-sand (500 mg, 22 mmol, from a paraffin suspension, washed with hexane) over a period of 4 days at 20 °C. Trimethylmethylenephosphorane[8] (270 mg, 23 % based on Eq. (6)) can be isolated from the volatile compounds of the reaction solution by fractional condensation. L_4CoH and $L_3Co[CH_2P(CH_3)_2]$ sublime from the residue at 80 °C/0.1 torr in an overall yield of *ca.* 60 %.

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Tri-*tert*-butylsilanes: Reactions and Hindered Si—C Rotation

By *Manfred Weidenbruch, Walter Peter*, and *Claude Pierrard*[*]

The reactions of tri-*tert*-butylsilane *(1)*[1–3] and the halosilanes *(2)* to *(4)*[1] readily preparable therefrom are largely determined by steric and electronic effects with the result that their Si—H and Si—Hal bonds differ markedly from those of other organosilanes.

$(t\text{-}C_4H_9)_3SiH$ *(1)* $(t\text{-}C_4H_9)_3SiCl$ *(2)* $(t\text{-}C_4H_9)_3SiBr$ *(3)* $(t\text{-}C_4H_9)_3SiI$ *(4)*

Only in exceptional cases are tri-*tert*-butylsilanes observed to react with nucleophiles, although this reaction, which usually proceeds with inversion of stereochemistry[4], is typical for this class of compounds. For instance, *(2)* fails to react with any of the following reagents: liquid or gaseous ammonia, sodium amide in boiling benzene, or lithium tetrahydridoaluminate in ether. Only under drastic conditions does reaction occur with solid potassium hydroxide in ethanol to give the silanol *(5)* in 82 % yield, which expectedly fails to condense to form disiloxane.

$$(t\text{-}C_4H_9)_3SiCl + KOH \xrightarrow[78\,°C,\ 2d]{C_2H_5OH} (t\text{-}C_4H_9)_3SiOH + KCl$$

(2) *(5)*

The usual methods for synthesis of organofluorosilanes by nucleophilic chlorine-fluorine exchange with SbF_3, ZnF_2, or Na_2SiF_6 are just as ineffective for *(2)* as the action of HF, SbF_3, or $(C_6H_5)_3CBF_4$ in the case of *(1)*. In contrast, the fluorosilane *(6)* is formed smoothly with the Lewis acid phosphorus pentafluoride.

$$(t\text{-}C_4H_9)_3SiH + PF_5 \xrightarrow{120\,°C} (t\text{-}C_4H_9)_3SiF + PF_3 + HF$$

(1) *(6)*

Generally, tri-*tert*-butylsilanes appear to react just as readily, or even faster, with electrophiles as comparable but sterically less hindered triorganosilanes. This is demonstrated especially clearly not only by halogenation reactions[1] but also by reactions with halocarbenes. Whereas *(1)* fails to undergo copper-catalyzed methylene insertion, dihalocarbenes, for which direct electrophilic attack on the Si—H bond has been established[5], give the insertion products *(7)* and *(8)* in 55 % yield each (Table 1).

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$$(1) + C_6H_5HgCX_3 \xrightarrow[\text{pet. ether}]{120\,^\circ C} (t\text{-}C_4H_9)_3SiCHX_2 + C_6H_5HgX$$

(7), X = Cl
(8), X = Br

Joint action of iodoform and potassium *tert*-butoxide on *(1)* at room temperature also appears to give initially the diiodomethyl derivative, which however decomposes to iodosilane *(4)* on attempted isolation by fractional sublimation. In the absence of base, *(1)* and iodoform undergo hydrogen-iodine exchange to give *(4)* only after prolonged heating in benzene.

Table 1. Tri-*tert*-butylsilanes $(t\text{-}C_4H_9)_3SiX$ *(5)*—*(8)* prepared.

Cpd.	X	M. p. [°C]	^{1}H-NMR ($CDCl_3$)	δ [ppm]
(5)	OH	34—38	1.12 (CH_3)	4.8 (SiOH)
(6)	F	36—38	1.10 (CH_3)	[a]
(7)	$CHCl_2$	205—210	1.30 (CH_3)	5.54 ($CHCl_2$)
(8)	$CHBr_2$	190—195	1.27 (CH_3)	5.24 ($CHBr_2$)

[a] ^{19}F-NMR (CCl_4): δ = 186.7 ppm.

Provided that the fourth substituent is sufficiently bulky the tri-*tert*-butylsilanes obtained permit the first direct proof of hindered rotation in simple alkylsilanes by ^{1}H-NMR spectroscopy. This restriction of free rotation, which has been thoroughly investigated for CC single bonds[6], has not previously been observed in the corresponding silicon compounds on account of the greater Si—C bond length.

In the case of hindered rotation about the Si—C bond the signal of the *tert*-butyl protons should be split into two singlets of relative intensity 2 : 1. That this assumption is correct follows from the low-temperature spectra of tri-*tert*-butyliodosilane *(4)* (Fig. 1).

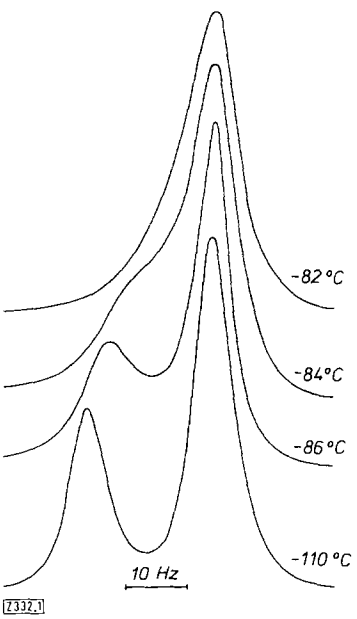

Fig. 1. Low-temperature ^{1}H-NMR spectra of tri-*tert*-butyliodosilane *(4)* (100 MHz).

On cooling of a solution of *(4)* in $CBrF_3$ the singlet of the *tert*-butyl protons at δ = 1.24 ppm becomes broader. In keeping with the slower rotation, splitting begins at −86 °C and continues until at −110 °C two isolated singlets appear at δ = 1.10 and 1.30 ppm in the intensity ratio of 2 : 1. The steric effectiveness of bromine or chlorine is less than that of iodine, with the result that signal splitting is only observed from −93 and −104 °C for compounds *(3)* and *(2)*, respectively. The activation parameters $\Delta G_C^{\ddagger}$ determined for *(2)*, *(3)*, and *(4)* by known methods[7] amount to 37.7, 39.6, and 40.8 kJ mol^{-1}, respectively.

The bulky dihalomethyl groups in *(7)* and *(8)* expectedly exert a highly pronounced influence on the rotation of the *tert*-butyl groups. The reduced symmetry and the additional restriction of free rotation about the Si—CHX_2 bond lead to complicated splitting patterns (first splitting below −74 and −68 °C, respectively) from which the activation parameters cannot be directly determined.

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(1), 18159-55-2; *(5)*, 56889-90-8; *(6)*, 56348-27-7; *(7)*, 57607-02-0; *(8)*, 57607-03-1

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Pentafluoroorthosulfuric Acid, $HOSF_5$

By *Konrad Seppelt*[*]

Sulfur rarely has the coordination number six, whereas it occurs more frequently in the case of selenium, and six is the dominating coordination number for tellurium. The SF_6 derivatives F—OSF_5[1] and $Cs^+OSF_5^-$[2] demonstrate the limits regarding the possible existence of six-coordinated sulfur compounds: the electronegativity of fluorine in $FOSF_5$ prevents an elimination reaction giving F_2 and SOF_4, while $ClOSF_5$ readily decomposes to ClF and SOF_4[3]. On the other hand, the salt $Cs^+OSF_5^-$ is stabilized by high lattice energy, whereas the lattice energy of $K^+OSF_5^-$ does not suffice for stabilization. Hence it was to be expected that $HOSF_5$ should decompose spontaneously into HF and SOF_4. However, this compound can actually be isolated pure, although it does indeed undergo the expected decomposition.

Pentafluoroorthosulfuric acid is prepared from $ClOSF_5$ by hydrolysis or—better—by reaction with hydrochloric acid:

$$ClOSF_5 + H_2O \xrightarrow[-60\,^\circ C]{HF} HOCl + HOSF_5 \qquad (1)$$

$$ClOSF_5 + HCl \xrightarrow{-95\,^\circ C} Cl_2 + HOSF_5 \qquad (2)$$

In reaction (1) $HOSF_5$ can be detected only by NMR spectroscopy, in reaction (2) this product is obtained as a white solid; chlorine and excess HCl can be completely removed by pumping at −95 °C. Pure $HOSF_5$ melts with decomposition to SOF_4 and HF at *ca.* −65 °C.

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The existence and structure of the thermally very sensitive pentafluoroorthosulfuric acid is confirmed by the following methods:

1. The ^{19}F-NMR spectrum (in $CHClF_2$, external standard $CFCl_3$) shows a typical AB_4 system ($\delta_A = -71.8$, $\delta_B = -67.0$ ppm), that differs from the spectrum of the starting compound $ClOSF_5$[3]. It is very similar to the spectrum of the homologous pentafluoroorthoselenic acid—this is not surprising, as structurally similar sulfur and selenium fluorides generally show almost identical NMR spectra[4, 5]. Thus the presence of four equatorial and one axial fluorine atom can be concluded; the proton is observed at $\tau = 2.9$ in the ^{1}H-NMR spectrum.

2. The mass spectrum does not show the molecular ion; the highest peak is, however, the fragment SF_5^+ ($m/e = 127$, 1%), which is accompanied by peaks for SOF_4^+ (124, 1%), SOF_3^+ (105, 100%), SF_3^+ (89, 8%), *etc.*, thus indicating that at least some $HOSF_5$ volatilizes without decomposition.

3. The Raman spectrum (in CH_3F, -120 °C) show bands at 3590 (νOH), 1080 (δOH), 761 ($\nu_s SF_4$), 635, 610 (νSF) and 530, 500 cm^{-1} (δSF). Considering the position and intensity of the peaks it very much resembles the spectrum of SF_6. Substitution of an F atom by an OH group leads to only slight deviations from the selection rule for octahedral symmetry—as is also found in the case of pentafluoroorthoselenic acid[6].

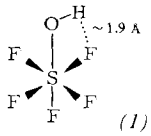
4. Identification of the decomposition products [cf. reaction (3)] is almost equivalent to an elemental analysis.

$$HOSF_5 \longrightarrow SOF_4 + HF \qquad (3)$$

$$HOSeF_5 \longleftarrow SeOF_4 + HF \qquad (4)$$

Reaction (3) proceeds slowly even at -78 °C; at -60 °C $HOSF_5$ has a halflife of *ca.* 15 min (determined by NMR spectroscopy).

The equilibrium of the HF elimination reactions (3) and (4) is shifted completely to the right in the case of sulfur and completely to the left in the case of selenium, once again confirming that selenium behaves more like tellurium (there is no monomeric $TeOF_4$; only the dimer $Te_2O_2F_8$ exists alongside the longer known $HOTeF_5$[5, 7]). The reason for the instability of $HOSF_5$ lies initially in the preferred formation of a sulfur-oxygen double bond (and formation of very stable HF). The decomposition at such a low temperature also suggests an exceptional kinetic instability.



(1)

As can be seen in a molecular model of $HOSF_5$ *(1)* the intramolecular distance H···F is so small (*ca.* 1.9 Å) that elimination of HF is particularly well favored. In $HOSeF_5$ rotation of the proton around the SeO axis is still hindered—as is seen from the vibrational spectrum[8]. Almost free rotation is finally observed in $HOTeF_5$.

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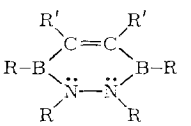
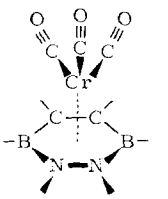
(1,2-Diaza-3,6-dibora-4-cyclohexene)tricarbonylchromium—A Complex with an η^6-$C_2B_2N_2$ Ligand[1]

By *Walter Siebert* and *Roland Full*[*]

The boron-carbon-nitrogen heterocycles isoelectronic to benzene and borazine are potential ligands for metal complexes. We report here on the ligand properties of one of the $C_2B_2N_2$ isomers, 4,5-diethyl-1,2,3,6-tetramethyl-1,2-diaza-3,6-dibora-4-cyclohexene *(1)*, whose synthesis[2] was achieved by reaction of 3,4-diethyl-2,5-dimethyl-1,2,5-thiadiborolene[3] with *N,N'*-dimethylhydrazine. The liquid, air-sensitive 6-electron donor *(1)* reacts with tris(acetonitrile)tricarbonylchromium with displacement of all three CH_3CN-ligands to give the red *hexahapto* complex *(2)*.



(1), R = CH_3, R' = C_2H_5



(2)

The mass spectrum[4] (70 eV) of *(2)* contains signals for the molecular ion $LCr(CO)_3^+$ [L = *(1)*] ($I_{rel} = 30$) and the following fragment ions: $LCrCO^+$(23), LCr^+(77), L^+(8), $\{L - CH_3\}^+$(51), $(CH_3)_4B_2N_2Cr^+$(100), $(C_2H_5)_2C_2Cr^+$(17), $(CH_3)_3BNCr^+$(74), Cr^+(99), CO^+(28).

While *(2)* can be described as "ethylenehydrazine"-tricarbonylchromium according to the 18-electron rule, *Wade*'s concept[5] (systemization of *closo*-, *nido*-, and *arachno*-structures) demands participation of the boron atom in the complex formation, since $n+2$ electron pairs are required for bonds between n skeletal atoms in a *nido* compound. In complex *(2)* the 2(7 + 2) electrons are provided by boron (2 × 2), carbon (2 × 3), and nitrogen (2 × 4). The expected interaction between the boron atoms and chromium atoms is evidenced by the

Table 1. Spectroscopic data for *(1)* and *(2)* [a].

Signal	I_{rel}	*(1)*	*(2)*
^{1}H-NMR, δ [ppm] *versus* TMS (in C_6D_6)			
B-CH_3	6 (s)	−0.75 (−0.62)	−0.67 (−0.57)
C-CH_3	6 (t) [c]	−1.21	−1.16
C-CH_2	4 (q)	−2.69	−2.4 [b]
N-CH_3	6 (s)	−2.95 (−2.91)	−2.45 (−2.50)
^{11}B-NMR, δ [ppm] *versus* $(C_2H_5)_2O \cdot BF_3$ (in C_6H_6)			
		−33.8 (−32.3)	−23.4 (−24.2)
IR, ν(CO) [cm^{-1}] (in C_6H_{12})			1959, 1880 (1963, 1867)

[a] Values for hexamethylborazine and hexamethylborazinechromium given in brackets for comparison.
[b] Multiplet resulting from magnetic non-equivalence of the CH_2 protons.
[c] $J = 7.8$ Hz.

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high-field shift of the ^{11}B-NMR signal (Table 1), which is consistent with the $\Delta\delta$ values (≈ 8 ppm) reported for the borazinetricarbonylchromium derivatives[6].

As in the corresponding hexamethylborazine compound[6], complex formation effects only a slight high-field shift for the BCH_3 protons in the ^{1}H-NMR spectrum of *(2)*, while the position of the NCH_3 signal is much more strongly influenced. Since the IR spectrum of *(2)*, like that of hexamethylbenzene-[7] and hexamethylborazinetricarbonylchromium[6], shows two CO bands (A_1, E), the local C_{3v} symmetry of the $Cr(CO)_3$ fragment is not disturbed by the $C_2B_2N_2$ ligand. Thus the new $C_2B_2N_2$—$Cr(CO)_3$ bonding system can be included in the series of *hexahapto*(6-electron donor-ligand)tricarbonylchromium complexes.

Experimental procedure:

A stirred mixture of tris(acetonitrile)tricarbonylchromium (1.74 mmol) and *(1)* (2.24 mmol) is heated at 90 °C under a stream of nitrogen for 1 h; stirring is then continued for a further 0.7 h at 90 °C/11 torr. After removal of excess *(1)* by distillation in a vacuum *(2)* can be recovered by sublimation at 120 °C/0.03 torr: red crystals, m.p. 111—112 °C (from hexane), yield 53 %.

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CAS Registry numbers:
(1), 57694-76-5; *(2)*, 57761-88-3; tris(acetonitrile)tricarbonylchromium, 6800-46-7

[1] Diboryl Compounds as Ligands in Metal Complexes, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 1: see Ref. [3].
[2] *R. Full* and *W. Siebert*, unpublished.
[3] *W. Siebert, G. Augustin, R. Full, C. Krüger*, and *Y.-H. Tsay*, Angew. Chem. *87*, 286 (1975); Angew. Chem. Int. Ed. Engl. *14*, 262 (1975).
[4] We thank Dr. *K. Steinbach* for the measurements.
[5] *K. Wade*, Chem. Commun. *1971*, 792; Adv. Inorg. Chem. Radiochem., in press.
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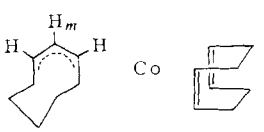
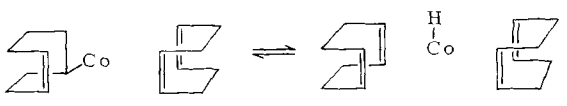
A Lithium-Cobalt Bimetal Complex

By *Helmut Bönnemann, Carl Krüger*, and *Yi-Hung Tsay*[*]

In their chemical behavior 1,5-cyclooctadiene(cyclooctenyl)-cobalt systems of type *(1)* or *(2)* are characterized by the extreme ease with which hydrogen can transfer from enyl ligand to cobalt atom and thus give rise to very reactive Co—H species, *e.g. (2a)*. This "mobile hydrogen" determines the catalytic mode of action of *(1)* and *(2)* toward olefins[1].



(1)



(2) *(2a)*

While *(2)* reacts quantitatively even at 0 °C with trimethylaluminum to form methane—whereby the hydride form *(2a)* was detected—the less reactive π form *(1)* is stable towards this reagent[1].

It has now been found, however, that *(1)* reacts under mild conditions with excess phenyllithium, the mobile hydrogen atom transferring from the cyclooctenyl- to the phenyl-group; the liberated benzene can be detected quantitatively. Between −10 and +20 °C a bimetallic complex of composition *(3)* is formed which is isolated from ethereal solution as golden-red crystals.

$$(1) + 2\ LiC_6H_5 \xrightarrow{(C_2H_5)_2O}$$

$$(C_8H_{12})_2CoLi(LiC_6H_5) \cdot 2\ (C_2H_5)_2O + C_6H_6$$

(3)

(3) is extremely sensitive towards oxygen; it immediately decomposes and turns black in air, but can be stored for long periods at room temperature. According to its NMR spectrum the compound is diamagnetic. From the extremely low conductivity (0.2 μS/cm in ether) it can be concluded that *(3)* is largely homopolar and not present as a dissociated ion pair. The IR spectrum (KBr mull in absence of air) contains numerous absorption bands, but some, typical for aromatic vibrations of free phenyllithium (*e.g.* at 1045, 1210 and 1040 cm^{-1}) are either lacking or strongly shifted; particularly noteworthy is a band, characteristic for the complex, at 1630 cm^{-1} in the region of C=C stretching vibrations. From the ^{1}H-NMR spectrum of *(3)* (100 MHz at 20 °C in [D_8]-THF with TMS as locking signal) it follows that the phenyl group is influenced to an extraordinary extent by the metal atoms, and that the ring current is strongly perturbed [signal shift of the *ortho* ($\tau = 2.47$) as well as *meta* and *para* protons ($\tau = 3.30$) to higher field strengths]. The signals of the coordinated eight-membered ring are likewise shifted upfield relative to *(1)*. The *meso* proton H_m of the starting compound *(1)* does not appear in the spectrum of *(3)*.

The X-ray structural analysis of *(3)* confirms that, surprisingly, the *meso* hydrogen is abstracted from the π-cyclooctenyl group during the action of phenyllithium on the coordinatively unsaturated complex *(1)*.

The crystal structure was deduced from 2371 reflections (329 classed as unobserved; $Mo_{K\alpha} = 0.71069$ Å) measured and refined by a special method ($a = 11.020(5)$, $b = 11.417(3)$, $c = 14.532(4)$ Å; $\alpha = 71.50(2)$, $\beta = 79.85(3)$, $\gamma = 58.44(3)°$; $P\bar{1}$; $Z = 2$; $R = 0.068$). Four coordination sites of the cobalt are occupied by three olefinic double bonds and one phenyl group. The lithium atoms occupy two further positions diametrically

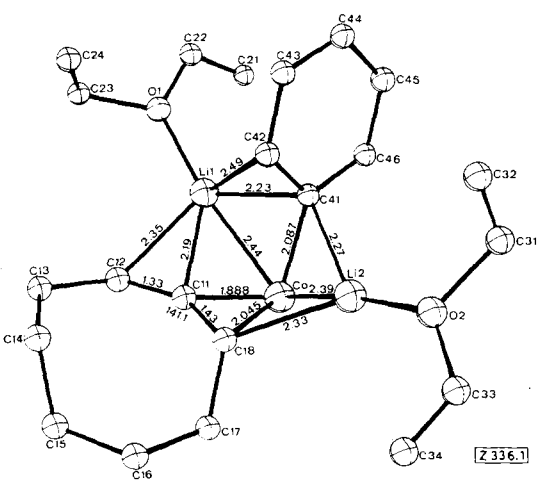


Fig. 1. Molecular structure of the bimetal complex *(3)* [the 1,5-cyclooctadiene ligands bound exclusively to the cobalt, with $d(C{=}C) = 1.39(1)$ and 1.40(1) Å, have been omitted].

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[**] X-ray structure analysis.

opposite each other relative to the cobalt atom. Free coordination sites on the lithium are occupied by ether molecules. Characteristic for interactions between main group metals and transition metals in complexes is the incorporation of carbon atoms with formation of multicenter electron-deficient bonds[2] (cf. Fig. 1).

The most important structural characteristics in *(3)* are multicenter bonds of the metals to the phenyl ring (C41) and to the second C_8 unit of the molecule. Noteworthy are the interactions between lithium and the β-C atoms of the phenyl group (C42)[3] as well as the C_8 unit (C12), and particularly the formation of a three-center bond with two different metal atoms at the olefin carbon atom C11 of the former cyclooctenyl group. The Co—C bond to the C11 atom (1.888 Å) is remarkably short.

Experimental procedure:

A stirred suspension of *(1)*[4] (10.0 g, 36.2 mmol) in diethyl ether (150 ml) is treated at −30 °C with a solution of LiC_6H_5 (6.1 g, 72.4 mmol) in ether (100 ml) and the whole warmed to 20 °C within 1 h. The color of the reaction solution gradually changes from dark-brown to red. After further stirring for 1.5 h the solution is evaporated down to *ca.* 150 ml and cooled to −80 °C, whereupon gold-red crystals of *(3)* separate out. Recrystallization from ether affords 8.5 g of the pure product, which is best stored in an ethereal atmosphere at −30 °C.

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[1] *H. Bönnemann*, Angew. Chem. *85*, 1024 (1973); Angew. Chem. Int. Ed. Engl. *12*, 964 (1973).
[2] *K. Jonas, D. J. Brauer, C. Krüger, P. J. Roberts*, and *Y.-H. Tsay*, J. Am. Chem. Soc., in press.
[3] *J. J. Brooks* and *G. D. Stucky*, J. Am. Chem. Soc. *94*, 7333 (1972); *J. J. Brooks, W. Rhine*, and *G. D. Stucky*, *ibid. 94*, 7339 (1972).
[4] *S. Otsuka* and *M. Rossi*, J. Chem. Soc. *A 1968*, 2630; *W. Leuchte*, Dissertation, Universität Bochum 1971; *H. Lehmkuhl, W. Leuchte*, and *E. Janssen*, J. Organometal. Chem. *30*, 407 (1971).

Ethylenebis(phenylsodium)nickel

By *Klaus Jonas*[*]

In continuation of our studies on alkali-metal compounds of nickel[1, 2] we have checked the reactivity of the (phenylsodium)nickel(0) system toward N_2[3] as well as other multibonded partners, *e.g.* olefins. In this communication we report on the complex ethylenebis(phenylsodium)nickel *(1)*, for which X-ray structural data are already available[5a].

Reaction of all-*trans*-1,5,9-cyclododecatrienenickel(0)[4] (CDT-Ni^0) with a salt free NaC_6H_5/LiC_6H_5 mixture (Na/Li = 2–4 : 1)[3] in the molar ratio $(NaC_6H_5 + LiC_6H_5)/Ni^0 = 2:1$ and ethylene in diethyl ether leads to the two compounds $(NaC_6H_5)_2NiC_2H_4[(C_2H_5)_2O]_2$ *(1a)* and $(LiC_6H_5)_2NiC_2H_4(C_2H_5)_2O$ *(2)*. The previously known complex *(2)* remains in solution, while the new sodium complex *(1a)* precipitates as an orange-red powder (yield 80—90 %).

$$2\,(m\,NaC_6H_5 + n\,LiC_6H_5) + CDT\text{–}Ni^0 \xrightarrow[(C_2H_5)_2O,\ 0\,^\circ C]{C_2H_4}$$

$$m\,(NaC_6H_5)_2NiC_2H_4[(C_2H_5)_2O]_2 + n\,(LiC_6H_5)_2NiC_2H_4(C_2H_5)_2O + CDT$$

(1a) *(2)*

$m/n = 2\text{–}4 : 1$

$m+n = 1$

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In *(1a)* the diethyl ether bonded to sodium can be replaced by stronger n-donors such as tetrahydrofuran (THF) or dimethoxyethane (DME) to give the crystalline complexes *(1b)* and *(1c)* etc.:

$$(1a) \xrightarrow{THF/(C_2H_5)_2O} [(NaC_6H_5)_2NiC_2H_4(THF)_{2.5}]_2 \quad (1b)$$

$$(1a) \xrightarrow{DME/(C_2H_5)_2O} (NaC_6H_5)_2NiC_2H_4(DME)_2 \quad (1c)$$

The composition of compounds *(1a)*, *(1b)* and *(1c)* follows from the nickel and sodium content (determined titrimetrically and by flame spectroscopy) and also by reaction of *(1)* with carbon monoxide, whereby the ethylene is quantitatively liberated. The various n-donors $(C_2H_5)_2O$, THF and DME in *(1a)*, *(1b)* and *(1c)* can be determined quantitatively by gas chromatography after decomposition of the complex with ethanol and distillation. The ^{1}H-NMR spectrum of *(1a)* in [D_8]-THF shows two groups of signals for the phenyl protons at $\tau = 1.9$ and 3.3 in the intensity ratio 4:6. The protons of the ethylene bound to nickel are, like those in the lithium complex *(2)* ($\tau = 9.87$)[1], strongly shielded, and in *(1a)* give rise to a singlet at $\tau = 9.58$.

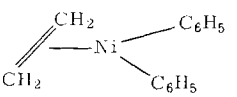
It follows from X-ray structural analysis of the ethylene complex *(1b)* and the (alkali-metal)nickel dinitrogen complexes

$$[\{(LiC_6H_5)_3Ni\}_2N_2\{(C_2H_5)_2O\}_{2\text{–}3}]_2 \quad (3)$$

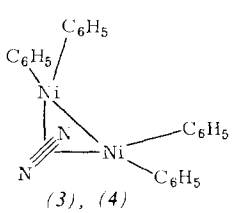
and

$$[C_6H_5\{NaO(C_2H_5)_2\}_2\{(C_6H_5)_2Ni\}_2N_2NaLi_6(OC_2H_5)_4O(C_2H_5)_2]_2 \quad (4)$$

that all three compounds contain characteristic diphenylnickel groups, which interact with the π system of the ethylene and the nitrogen to give a trigonal array of these ligands. The various interactions of the alkali metal atoms have tentatively been ignored in this connection. Whereas only one $(C_6H_5)_2Ni$ group is coupled with the C_2H_4 ligand in complex *(1b)*[5a],



(1b)



(3), *(4)*

in complexes *(3)*[5b] and *(4)*[3] two $(C_6H_5)_2Ni$ groups are bonded side-on to the N_2 ligand *via* the two nickel atoms.

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CAS Registry numbers:
CDT-Ni^0, 12126-69-1; NaC_6H_5, 1623-99-0;
$(NaC_6H_5)_2NiC_2H_4[(C_2H_5)_2O]_2$, 57774-32-0

[1] *K. Jonas*, Angew. Chem. *85*, 1050 (1973); Angew. Chem. Int. Ed. Engl. *12*, 997 (1973).
[2] *K. Fischer, K. Jonas, P. Misbach, R. Stabba*, and *G. Wilke*, Angew. Chem. *85*, 1002 (1973); Angew. Chem. Int. Ed. Engl. *12*, 943 (1973).
[3] *K. Jonas, D. J. Brauer, C. Krüger, P. J. Roberts*, and *Y.-H. Tsay*, J. Am. Chem. Soc., in press.
[4] *B. Bogdanović, M. Kröner*, and *G. Wilke*, Justus Liebigs Ann. Chem. *699*, 1 (1966).
[5] a) *D. J. Brauer, C. Krüger, P. J. Roberts*, and *Y.-H. Tsay*, Angew. Chem. *88*, 52 (1976); Angew. Chem. Int. Ed. Engl. *15*, 48 (1976); b) *C. Krüger* and *Y.-H. Tsay*, *ibid. 85*, 1051 (1973), and *12*, 998 (1973).

Structure of a Bimetal-Ethylene Complex: $[(C_6H_5)_2NiC_2H_4]_2Na_4(THF)_5$

By *David J. Brauer, Carl Krüger, Paul J. Roberts,* and *Yi-Hung Tsay*[*]

Recently, *Jonas*[1] reported the preparation of side-on π-complexes of molecular nitrogen with alkali metal compounds of nickel. In our structural investigations of such bimetallic systems[2, 3] we carried out an X-ray structural analysis of a complex having the composition $C_{48}H_{68}Na_4Ni_2O_5$, which could be obtained from a nitrogen-containing intermediate by crystallization from a diethyl ether/tetrahydrofuran (THF)

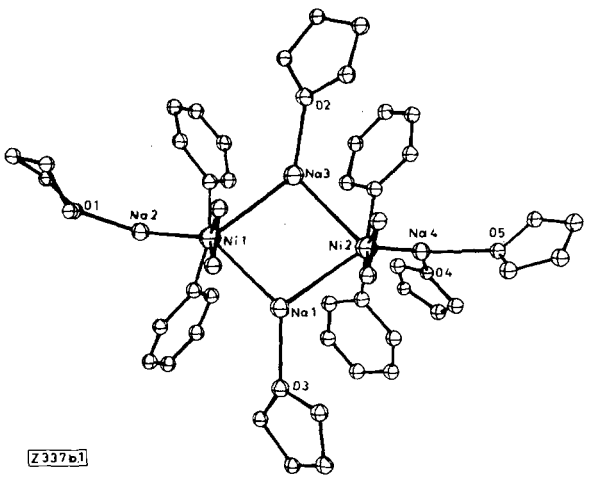

Fig. 1. Molecular structure of the complex $[(C_6H_5)_2NiC_2H_4]_2Na_4(THF)_5$.

mixture, as well as by direct synthesis[1]. The red substance crystallizes in the triclinic system (unit cell: $a=9.779(2)$, $b=12.884(3)$, $c=20.811(6)$ Å; $\alpha=94.29(2)$, $\beta=93.05(2)$, $\gamma=104.25(2)°$; space group $P\bar{1}$; $Z=2$). The structure (Fig. 1) was solved by the heavy atom method, from 4024 (1488 unobserved) reflections, with the aid of a phase refinement process and refined to an R value of 0.0742 ($R_w=0.0909$).

The molecule is formally composed of two $(Ph_2NiC_2H_4)$ units and four $Na(THF)_x$ groups ($x=1$ or 2). Characteristic for Ni^0 is the trigonal arrangement of the organic ligands (two σ-bonded[4] phenyl groups and one π-bonded ethylene molecule). The dihedral angles between the plane of the σ-bond ($NiPh_2$) and the plane of the π-bond (NiC_2H_4) in both parts of the molecule are 6.4 and 7.7° in the same direction. Two bridging sodium atoms are bonded to nickel almost perpendicularly to the trigonal plane and give rise to a Ni—Na—Ni—Na four-membered ring. The two nickel atoms are each bonded with a further sodium atom outside of the ring. Additional ion-pair bonding can be detected between these sodium ions and the α-C atoms of the phenyl groups[5] (Na—C 2.56—2.68 Å). Free coordination sites on all Na atoms are occupied by THF; the Na atoms in the ring can bond only one THF molecule whereas those outside of the ring are capable of bonding two THF molecules. However, this possibility is utilized in only one case. Na2 takes up only one THF ligand (Fig. 1) and in addition forms a new type of intermolecular bridge to an ethylene unit of a neighboring complex molecule. This gives rise to a polymeric chain structure in the lattice (cf. Fig. 2), with Na2 at the rear of the Ni-olefin π bond (Na—C 2.75, 2.66 Å). Furthermore, a weak ion-pair interaction is detectable between the Na atoms in the four-membered ring (Na1, Na3) and the CH groups of the olefin. As also in the Ni—C bond lengths of the complexed olefin, this result is only slightly, if at all, reflected in the C—C bond length (C—C 1.45(2) and 1.43(2) Å).

We interpret the formation of the planar metal-metal four-membered ring as resulting from the development of two

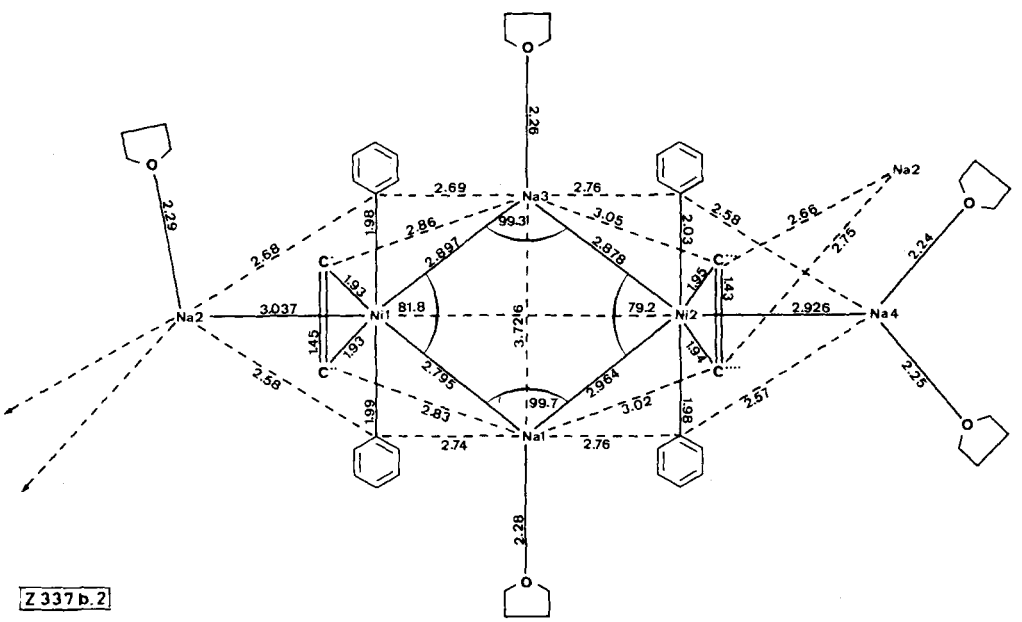

Fig. 2. Bond lengths [Å] and angles [°] in crystalline $[(C_6H_5)_2NiC_2H_4]_2Na_4(THF)_5$.

three-center electron-deficient bonds between Ni and Na^+, with the observed apical angles of 79.2 and 81.8° at the nickel atoms. A weak transannular Na—Na interaction (3.726 Å) cannot be ruled out[6]. No bonding exists, however, between the two Ni atoms (Ni—Ni 4.303 Å).

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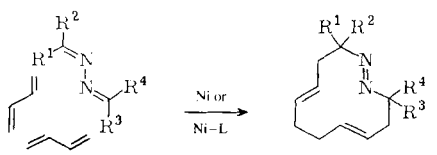
CAS Registry numbers:
$[(C_6H_5)_2NiC_2H_4]_2Na_4(THF)_5$, 57774-33-1

[1] *K. Jonas*, Angew. Chem. *88*, 51 (1976); Angew. Chem. Int. Ed. Engl. *15*, 47 (1976); *ibid. 85*, 1050 (1973) and *12*, 997 (1973).
[2] *C. Krüger* and *Y.-H. Tsay*, Angew. Chem. *85*, 1051 (1973); Angew. Chem. Int. Ed. Engl. *12*, 998 (1973).
[3] *K. Jonas, D. J. Brauer, C. Krüger, P. J. Roberts*, and *Y.-H. Tsay*, J. Amer. Chem. Soc., in press.
[4] *K. Fischer, K. Jonas, P. Misbach, R. Stabba*, and *G. Wilke*, Angew. Chem. *85*, 1002 (1973); Angew. Chem. Int. Ed. Engl. *12*, 943 (1973).
[5] *E. Müller, J. Krausse*, and *K. Schmiedeknecht*, J. Organometal. Chem. *44*, 127 (1972).
[6] Na—Na: 3.7157 Å in the metal, 3.079 Å in the gas phase.

Catalytic Synthesis of 1,2-Diaza-1,5,9-cyclododecatrienes from Butadiene and Azines

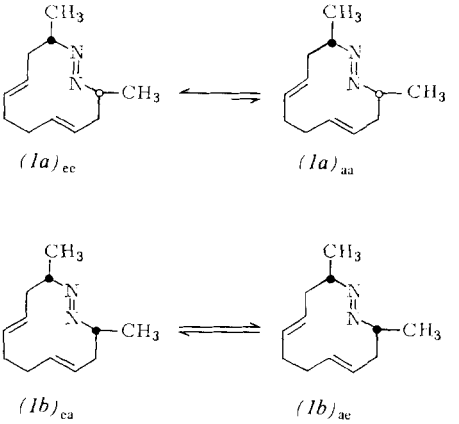
By *Paul Heimbach, Bernard Hugelin, Heinz Peter, Achim Roloff*, and *Eduard Troxler*[*]

Starting points in our investigations were, *inter alia*, publications by *Wilke*[1] and *Heimbach*[2] as well as an observation by *Meyer*[3]. We have now found, in independent studies[4, 5], that 3,3,12,12-substituted 1,2-diaza-1,5,9-cyclododecatrienes *(1)*—*(12)* are formed by catalytic co-oligomerization of ketazines or aldazines with butadiene. We employed nickel catalysts with and without added phosphane or phosphite; the molar ratio of butadiene to azine was 3:1 to 10:1 (see Table 1)[6].



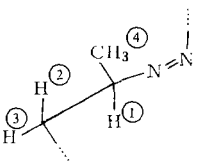
(1)-*(12)*

equatorially, while in the case of the *cis* compound *(1b)* the forms $(1b)_{ea}$ and $(1b)_{ae}$ are in equilibrium.



$(1a)_{ee}$ $(1a)_{aa}$ $(1b)_{ea}$ $(1b)_{ae}$

(1a) and *(1b)* differ greatly from each other, *inter alia*, in the coupling constants of the ^{1}H-NMR spectra. This is clearly seen from a section of the spectrum of the rigid form $(1a)_{ee}$:



Rigid form $(1a)_{ee}$:
$J_{1,2}=11$ Hz; $J_{1,3}=2$ Hz; $J_{1,4}=6.5$ Hz

Flexible forms $(1b)_{ea}$ and $(1b)_{ae}$:
$J_{1,2}=6.5$ Hz (mean value: $11+2$); $J_{1,3}=4$ Hz (mean value); $J_{1,4}=6.5$ Hz.

The IR spectrum of *(1a)* and *(1b)* shows only typical bands for *trans* double bonds (at 1670 and 956 cm^{-1}). A band at 1675 cm^{-1} in the Raman spectrum is indicative of a *trans* arrangement of the —N=N— grouping. If cyclic ketones are used for the synthesis of symmetric ketazines ($R^1=R^2=R^3=R^4=$ alkyl) di-spiro compounds such as *(12)* are formed on co-oligomerization with butadiene.

All compounds were identified and characterized by elemental analysis and ^{1}H-NMR, IR, Raman, and mass spectra.

Table 1. Prepared 1,2-diaza-1,5,9-cyclododecatrienes *(1)*—*(12)*. The yields are based on azine used. Molar ratio butadiene: azine = 3–10:1. Catalyst: see experimental procedure.

Cpd.	Substituents	Reaction temp. [°C]	Reaction time [h]	Yield [%]	B.p. [°C/torr] M.p. [°C]
(1)	$R^1=R^3=CH_3$; $R^2=R^4=H$	80	4	83	110/10 [a]
(2)	$R^2=R^3=CH(CH_3)_2$; $R^2=R^4=H$	80	4	72	89–92/0.03
(3)	$R^1=R^3=n$-C_7H_{15}; $R^2=R^4=H$	90	0.66	16	60–61 [b]
(4)	$R^1=R^3=c$-C_6H_{11}; $R^2=R^4=H$	60	1	79	102–103 [b]
(5)	$R^1=R^3=p$-CH_3—C_6H_4; $R^2=R^4=H$	30	48	78	155 [b]
(6)	$R^1=R^3=p$-F—C_6H_4; $R^2=R^4=H$	80	2.5	50	156 (dec.) [b]
(7)	$R^1=R^3=p$-$(CH_3)_2N$—C_6H_4; $R^2=R^4=H$	80	1.5	84	182, 134 [c]
(8)	$R^1=R^3=$ 3-Br-4-CH_3O—C_6H_3; $R^2=R^4=H$	35	20	80	124 [b]
(9)	$R^1=R^3=$ 1-Methyl-2-pyrrolyl; $R^2=R^4=H$	35	21	82	138—140 [b]
(10)	$R^1=R^2=R^3=R^4=CH_3$	80	4	93	63–65/0.02
(11)	$R^1=R^3=CH_3$; $R^2=R^4=C_2H_5$	90	0.66	55	103–104/0.4
(12)	R^1—$R^2=R^3$—$R^4=-(CH_2)_5-$	60	1	52	62–64

[a] $(1a):(1b)=5.6:1$.
[b] Only one isomer was prepared in pure form on recrystallization.
[c] Two isomers in the ratio 2.8:1.

The symmetric aldazines ($R^1=R^3=$ alkyl or aryl; $R^2=R^4=H$) lead to two isomers; for instance, the *trans* compound *(1a)* is present almost exclusively in the practically rigid conformation $(1a)_{ee}$ with both substituents arranged

3,12-Dimethyl-1,2-diaza-1,5,9-cyclododecatriene (1)

A mixture of bis(2,4-pentanedionato)nickel (3.1 g; 12 mmol) and triphenylphosphane (3.2 g; 12 mmol) was treated with toluene (42.7 g) under inert gas in a 500 ml ampoule and

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reduced with ethoxydiethylaluminum (3.25 g; 25 mmol) at 0 °C. The color of the solution changed from green to red. A mixture of acetaldehyde azine (47.8 g; 0.5 mol), butadiene (83 g; 1.54 mol), and toluene (77 g) is prepared and added to the catalyst solution. A contraction in volume of *ca.* 10% is observed within 24 h at 40 °C. Deactivation of the catalyst with an equivalent amount of sulfur and subsequent distillation at 10^{-4} torr affords 98 g of *(1)* (83% yield w.r.t. azine used). Separation into the isomers *(1a)* and *(1b)* was achieved by preparative gas chromatography.

100-MHz ^{1}H-NMR (solvent [D_8]-toluene): *(1a)*, $\tau = 5.05$ (m), 6.16 (m), 7.47—7.56 (m), 8.12 (m), 8.89 ppm (d) (4:2:4:4:6); *(1b)*, $\tau = 5.07$ (m), 6.65 (m), 7.44—7.89 (m), 8.30 (m), 8.85 ppm (d) (4:2:4:4:6).

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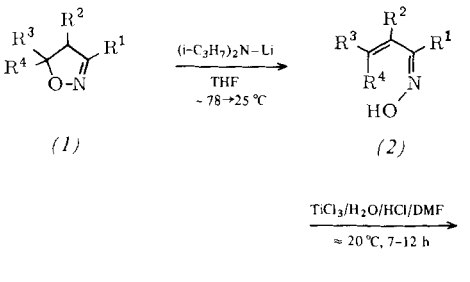
[5] *A. Roloff* and *P. Heimbach*, unpublished.
[6] If the carbon atoms of 1,3-dienes are substituted by nitrogen, the perturbation of the reactive centers 1 and 4 will be lowest when the nitrogen is present in positions 2 and 3.

been exploited[2]. Such use requires the availability of methods for retransforming 2-isoxazolines into open-chain products.

We now describe the conversion of substituted isoxazolines *(1)* into unsaturated oximes *(2)* and thence into enones *(3)*. Treatment of 3,5-diphenyl-2-isoxazoline *(1c)* with ethylmagnesium bromide (molar ratio 1:2) at 80–85 °C in diglyme affords a 30% yield of the ring cleavage product (*E,E*)-chalcone oxime *(2c)*. The yield of crystalline *(2c)* increases on use of butyllithium, or even better lithium diisopropylamide, to 60%. The unsaturated oximes *(2)* listed in Table 1 are obtained similarly, each in one stereoisomeric form only (according to the NMR spectra the crude products are also isomerically pure).



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

The crude products *(2)* of ring cleavage can be converted directly and smoothly at room temperature into enones *(3)*

Table 1. α,β-Unsaturated oximes *(2)* and enones *(3)* from 2-isoxazolines *(1)*. The structures of compounds *(2)* and *(3)* [new: *(2b)* and *(2e)*] were established by IR and NMR spectra and by correct elemental analyses.

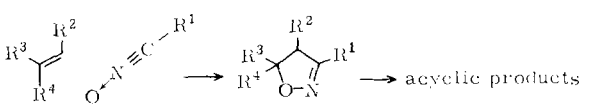
Starting compound	R^1	R^2	R^3	R^4	*(2)* yield [%]	*(2)* m. p. [°C]	*(3)* yield [%] [a]	*(3)* m. p. [°C] b. p. [°C/torr] [d]
(1a)	CH_3	H	C_6H_5	H	37 [b]	102	42	39—40
(1b)	C_2H_5	H	C_6H_5	H	60 [b]	114	59	36—37
(1c)	C_6H_5	H	C_6H_5	H	60 [b]	114—115	59	53—55
(1d)	C_6H_5	H	C_6H_5	CH_3	60	124—126	93 [c]	125—130/$\approx 10^{-3}$
(1e)	C_6H_5	—$(CH_2)_3$—		H	61	94	70	95/$\approx 10^{-3}$
(1f)	CH_3	—$(CH_2)_3$—		H	—		—	

[a] Yield based on *(1)*. Compounds *(2)* were not isolated.
[b] Acetophenone is formed (NMR, 5—9%) in a fragmentation occurring as side reaction [4].
[c] Mixture of (*E*), (*Z*), β,γ in the ratio 87:4:9 (NMR).
[d] Bulb-tube distillation, bath temperature.

Eliminative Ring Opening of 2-Isoxazolines: A New Route to α,β-Unsaturated Ketones[**]

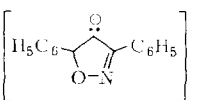
By *Volker Jäger* and *Hartmut Grund*[*]

Substituted 2-isoxazolines (4,5-dihydroisoxazoles) *(1)* are readily accessible under mild conditions by 1,3 dipolar cycloaddition of nitrile oxides to alkenes[1]. This represents a CC bond forming process in which a substituted C_1 unit (nitrile oxide) is combined with a (substituted) C_2 unit (alkene). By suitable choice of reactants, which can be varied within wide limits, a large number of carbon skeletons can be constructed. However, synthetically the inherent possibilities have hardly



(1)

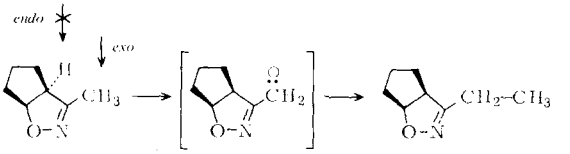
by treatment with an excess of titanium(III) chloride (15% aqueous solution in 4% hydrochloric acid to which has been added an equal volume of dimethylformamide)[3] (see Table 1).



(4c)

endo-anion

The oxime formation occurs *via endo* anion *(4)*[5–8] as shown, for example, by deuterolysis of *(4c)*. If *exo* hydrogen atoms are present in the α position of the CN double bond in *(1)*, then *exo* metalation competes with *endo* metalation/ring cleavage (cf. yields in Table 1). Depending upon the degree of substitution of the *exo* and *endo* positions this should also permit selective CC bond formation *at the isoxazoline stage* and therefore considerably



(1f) *exo*-anion *(1g)*

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enhance the synthetic utility of the 2-isoxazolines. This is illustrated by the reaction of *(1f)* with lithium diisopropylamide, which does not give a ring cleavage product (see Table 1), but affords the 3-ethyl derivative *(1g)* (*exo* alkylation) in >70% yield after addition of methyl iodide.

2-Isoxazolines thus represent latent[6] enones, similar to isoxazoles[6, 9] and isoxazolidines[6]. The scope of the reported acylation sequence remains to be determined; it circumvents carbocationic intermediates and its direction is governed mainly by steric factors, as is usual with nitrile oxide cycloadditions[1].

Conversion of isoxazolines (1) into enones (3):

Compound *(1)* (10 mmol) dissolved in anhydrous THF (10 ml) is slowly added dropwise at −78 °C to a solution of lithium diisopropylamide [from 1.11 g ≙ 10.9 mmol of amine in anhydrous THF (20 ml) and 7.6 ml ≙ 12.1 mmol of *n*-butyllithium in hexane]. After two hours the reaction mixture is allowed to warm slowly to room temperature and hydrolyzed with glacial acetic acid (1.4 ml, ≈23 mmol) and subsequently with saturated sodium chloride solution (20 ml). It is then extracted with three portions of dichloromethane. The combined extracts are washed with water and filtered through a short column packed with sodium sulfate. The solvent is removed and the residue is dissolved in dimethylformamide (50 ml), treated with a solution of titanium(III) chloride (50 ml, 15% in 4% hydrochloric acid), and stirred for 7 to 12 h at room temperature. After addition of water (100 ml) the reaction mixture is extracted three times with ether, the extracts are washed (water, saturated sodium hydrogen carbonate solution, water) and dried over sodium sulfate. Removal of the solvent is followed by bulb tube distillation (10^{-3} to 10^{-1} torr) and crystallization from light petroleum (where necessary with addition of ether) at −30 °C.

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(3-Siloxy-3-buten-1-ynyl)amines

By *Gerhard Himbert*[*]

Ynamines add to the CC and the CO double bond of ketenes with formation of 3-aminocyclobutenones and allenecarboxamides, respectively[1]. The latter are interpreted as isomerization products of initially formed oxete derivatives.

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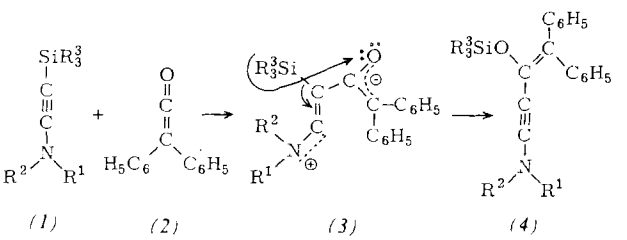
β-Silylated ynamines *(1)*[2], however, are able to follow a different reaction path, as is shown for example by their reaction with diphenylketene *(2)*. At the intermediary stage of the zwitterion *(3)* formation of the four-membered carbocycle and heterocycle is circumvented and a [1,3] silyl shift to the oxygen atom takes place affording the novel (3-siloxy-3-buten-1-ynyl)amines *(4)* (see Table 1)[3], in which the ynamine function is retained. The driving force behind this rearrangement might be the high Si—O bond energy[4].



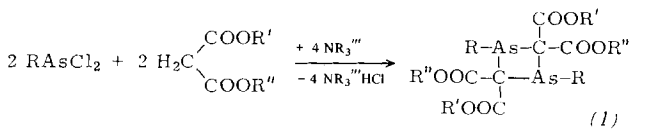
(1) *(2)* *(3)* *(4)*

Table 1. Prepared (3-siloxy-3-buten-1-ynyl)amines *(4)*.

(4)	R^1	R^2	R^3	Yield [%]	M.p. [°C]	IR [a]
a	C_2H_5	C_2H_5	CH_3	68	[b]	2216
b	CH_3	C_6H_5	CH_3	76	77—79	2218
c	C_6H_5	C_6H_5	CH_3	61	80—82	2218
d	C_2H_5	C_2H_5	C_6H_5	85	92—95	2210
e	CH_3	C_6H_5	C_6H_5	66	138—140	2216
f	C_6H_5	C_6H_5	C_6H_5	64	159—160	2235

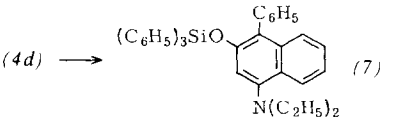
[a] IR (film or Kbr), C≡C absorption.
[b] B.p. 158—165 °C/0.4 torr (bulb-tube distillation).

Appearance of the C≡C and C=C absorptions in the IR spectrum (Table 1) and of the molecular ion M^+ in the mass spectrum lends support to the constitution of the new enynamines. Further support is provided by the fact that hydrolysis and desilylation affords the 3-siloxy-3-buteneamides *(5)* and the acetoacetamides *(6)*.



(1)

N,N-Diethyl[4,4-diphenyl-3-(triphenylsiloxy)-3-buten-1-ynyl]amine *(4d)* rearranges in $CDCl_3$ within 3—4 days with quantitative loss of the CC triple bond into an isomeric compound, whose spectroscopic and analytical data are consistent with the naphthalene structure *(7)*. [^{1}H-NMR ($CDCl_3$): δ = 0.82 (t, $NCCH_3$, J = 7 Hz), 2.89 (q, N—CH_2, J = 7 Hz), 6.74 (s, 2-H)—MS (70 eV): m/e = 549 (100%, M^+), 534 (47%), 259 (73%)].



(7)

N-Methyl-N-phenyl-[4,4-diphenyl-3-(trimethylsiloxy)-3-buten-1-ynyl]amine (4b)

A solution of *(1b)*[2a] (4.06 g, 20 mmol) in ether (50 ml) is treated with diphenylketene (3.88 g, 20 mmol) in ether[5] over a period of 10 min at −30 °C and the whole stirred for a further 2 h at room temperature. The solvent is then removed under reduced pressure and the residue taken up in

50 ml petroleum ether (40–70 °C). After cooling to −70 °C and rubbing, *(4b)* precipitates out as almost colorless crystals.

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CAS Registry numbers:
(1a), 33567-68-9; *(1b)*, 33567-67-8; *(1c)*, 33567-66-7; *(1d)*, 57694-91-4; *(1e)*, 57694-92-5; *(1f)*, 57694-93-6; *(2)*, 525-06-4; *(4a)*, 57694-69-6; *(4b)*, 57694-70-9; *(4c)*, 57694-71-0; *(4d)*, 57694-72-1; *(4e)*, 57694-73-2; *(4f)*, 57694-74-3; *(7)*, 57694-75-4

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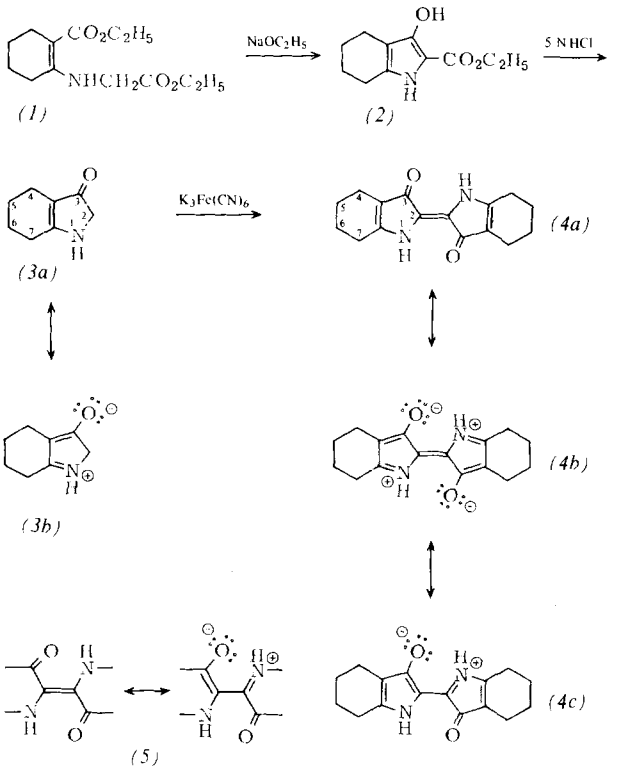
[2] For the preparation of these ynamines see a) *J. Ficini* and *A. Duréault*, C. R. Acad. Sci. Ser. *C 273*, 289 (1971); b) *L. L. Shchukovskaya, L. D. Budakova*, and *R. J. Pal'chik*, Zh. Obshch. Khim. *43*, 1989 (1973); Chem. Abstr. *80*, 15001 b (1974); c) *G. Himbert, D. Frank*, and *M. Regitz*, Chem. Ber., in press.

[3] Acylketenes, because of their "diene structure", can also avoid this formation of a four-membered ring and instead undergo Diels-Alder reaction to give the 4-pyrones; see Ref. [1b].

[4] *W. Noll*: Chemie und Technologie der Silicone. 2nd edition, Verlag Chemie, Weinheim 1968, p. 265.

[5] When the addition is performed the other way round contamination with the 2:1 adduct is observed; a second ketene molecule adds to the initially formed *(4)* with predominant formation of cyclobutenone derivatives.



Octahydroindigo[**][1]

By *Georg Pfeiffer, Walter Otting*, and *Helmut Bauer*[*]

4,4',5,5',6,6',7,7'-Octahydroindigo *(4)*, which cannot be synthesized by reduction of indigo[2], is prepared in the following manner:

The condensation product *(1)* obtained from ethyl 2-oxo-1-cyclohexanecarboxylate and glycine ethyl ester is subjected to Dieckmann cyclization to give *(2)*. Acid hydrolysis of *(2)* in refluxing 5 N HCl proceeds with concomitant decarboxylation to 4,5,6,7-tetrahydroindoxyl *(3)*. This method represents an improved and generally applicable route to 4-oxo-2-pyrrolines[3, 4]. Compound *(3)* exhibits a UV spectrum [λ_{max} ($CHCl_3$) = 314 nm ($\log\varepsilon = 4.28$)] and an IR spectrum [in $CHCl_3$: 3445 s, 1655 s, 1575 s cm^{-1}] typical of amino enones[5] and, according to its NMR spectrum, exists in the oxopyrroline form *(3a)*. Both resonance forms *(3a)* and *(3b)* participate in the ground state.

Oxidation of *(3)* with $K_3Fe(CN)_6$ at pH 7 affords the dark violet octahydroindigo *(4)*, which is a pyrroleindigo soluble in organic solvents. In aqueous methanolic solution *(4)* can be vatted with $Na_2S_2O_4$ and reoxidized by air. Since a considerable proportion is destroyed by oxidation in this process as well as in the methods generally employed for dyeing cotton, compound *(4)* is hardly suitable for use as a vat dye. Unlike indigo, octahydroindigo *(4)* is very readily deprotonated and protonated, respectively, in alkaline and acid methanolic solution, the color changing to yellow. Deprotonation is rapidly followed by autoxidation.

The electronic spectrum of *(4)* [λ_{max} ($CHCl_3$) = 315 nm ($\log\varepsilon = 4.38$; 520 (4.11)] is analogous to that of tetramethylpyrroleindigo[3, 6], which is however, far less soluble than *(4)*. Thus the "partial hydrogenation" of the two annelated benzene rings of indigo [λ_{max} ($CHCl_3$) = 607 nm] leads to hypsochromic shift of the longest wave absorption maximum by 87 nm. The longest wave absorption maximum of *N,N'*-dimethyloctahydroindigo [λ_{max} ($CHCl_3$) = 582 nm] obtained by methylation of *(4)* shows a hypsochromic shift of 68 nm relative to that of *N,N'*-dimethylindigo [λ_{max} ($CHCl_3$) = 650 nm].

In contrast to the IR spectrum of indigo, that of *(4)* [in $CHCl_3$: 3410 m, 1630 m, 1560 vs cm^{-1}] is distinguished by the very intense band at 1560 cm^{-1}. In this respect, *(4)* resembles the amino enones which all exhibit a similarly strong band in this region. Thus not only the resonance form *(4c)* but also the form *(4b)* analogous to *(3b)* probably contribute to the ground state of *(4)*. The resonance form *(4c)* results from the presence of the fundamental indigo chromophore system *(5)*[7], which no longer exhibits any features of amino enones. Accordingly, octahydroindigo *(4)* possesses both indigo and amino enone character on account of the structural elements *(5)* and *(3)*. This overlapping of characteristics also follows from data calculated by the PPP[7] and MINDO/2 methods[8], which require, *e.g.*, a more pronounced positive character of the nitrogen atoms and a lower C=O bond order in *(4)* than in *(3)* and *(5)*.

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[**] Financial support of this work by the Fonds der Chemischen Industrie is gratefully acknowledged.

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[2] *B. Robinson*, Chem. Rev. *69*, 789 (1969), see page 795.
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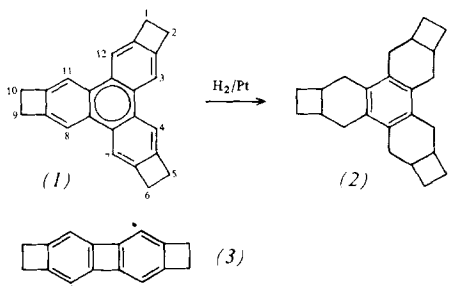
[6] *H. Bauer*, Angew. Chem. *80*, 758 (1968); Angew. Chem. Int. Ed. Engl. *7*, 734 (1968).
[7] *E. Wille* and *W. Lüttke*, Angew. Chem. *83*, 853 (1971); Angew. Chem. Int. Ed. Engl. *10*, 803 (1971); Chem. Ber. *106*, 3240 (1973).
[8] *H. Vogler, G. Pfeiffer*, and *H. Bauer*, unpublished.

10,11-Dihydrocyclobuta[*b*]triphenylene and 1,2,5,6,-9,10-Hexahydrotriscyclobuta[*b,h,n*]triphenylene[**]

By *R. L. Funk* and *K. P. C. Vollhardt*[*]

The synthesis and properties of various aromatic carbocycles fused to one strained ring have been the subject of considerable recent research activity. There are considerably fewer structures known consisting of two strained rings fused to an aromatic system. We now wish to report the synthesis of 1,2,5,6,9,10-hexahydrotriscyclobuta[*b,h,n*]triphenylene *(1)*, a benzenoid tetracycle to which *three* strained rings are symmetrically fused[1].



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

Treatment of a concentrated (1.2 M) solution of 4-bromo-5-iodo-1,2-dihydrocyclobutabenzene with magnesium (room temperature; 12 h) leads to a complex mixture of halogenated coupled products, in addition to the biphenylene derivative *(3)* and the desired triphenylene derivative *(1)*[2]. The new cyclobutaarene *(1)* was obtained after repeated preparative thin layer chromatography on silica (3% ether in pentane) and fractional crystallization from ether as colorless plates (yield 0.5%) which decomposed above 260 °C without melting. The structural assignment is based on the spectral and chemical properties [MS: $m/e = 306.1406$ (calcd. 306.1408), M^+; ^{1}H-NMR ($CDCl_3$): $\tau = 1.70$ (s), 6.57 (s); electronic spectrum: Fig. 1]. Hydrogenation with Pt (in ethanol) proceeds unusually rapidly to the partially hydrogenated benzene derivative *(2)*[2,6], a colorless oil [^{1}H-NMR (CCl_4): $\tau = 6.6$—8.3 (m); UV (ether): $\lambda_{max} = 227$ sh, 238 sh, 270].

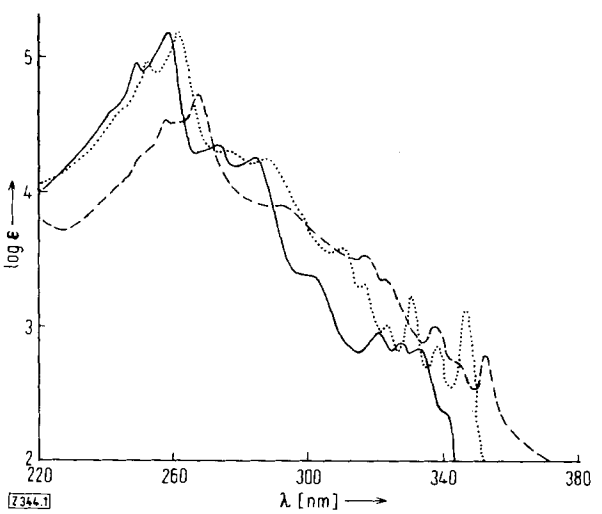


Fig. 1. Electronic spectra of triphenylene (——), *(4)* (·····), and *(1)* (– – –) in 95% ethanol.

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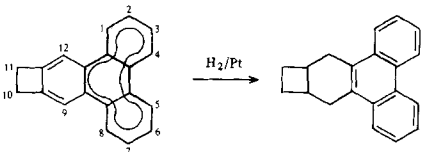
For comparison model *(4)* with one annelated cyclobutane ring (10,11-dihydrocyclobuta[*b*]triphenylene) was prepared by the iodine catalyzed oxidative photocyclization[3] of 4,5-diphenyl-1,2-dihydrocyclobutabenzene[4] followed by preparative thin layer chromatography (yield 82%, 38% conversion; m.p. 168—169 °C). The structure assignment is based on the physical and chemical properties. Hydrogenation (Pt) leads to the phenanthrene derivative *(5)*[2] [m.p. 151—152 °C].



(4) *(5)*

The increasing strain in the series triphenylene, *(4)* and *(1)* is reflected in the physical and chemical properties of these compounds. Thus, fusing one cyclobutane ring to triphenylene seems to lead to increased bond localization in one benzene ring as indicated in structure *(4)*. This is evidenced by the chemical shift for 4-H, 5-H ($\tau = 1.32$), intermediate between the corresponding absorptions in the phenanthrene derivative *(5)* ($\tau = 1.25$) and triphenylene ($\tau = 1.44$)[5,7], the relatively high chemical shift for 9-H, 12-H ($\tau = 1.60$) and the ease of hydrogenation of *(4)*[6]. Fusion of three cyclobutane rings seems to result in increased bond fixation as suggested in formula *(1)*. The aromatic signals are shifted an additional 0.1 ppm to higher field due to the cumulative influence of three four-membered rings[7], and hydrogenation is rapid[6] but leaves the central benzene ring intact. This is, of course, in striking contrast to the stringent conditions required to hydrogenate triphenylene[9]. Finally, the electronic spectra (Fig. 1) exhibit strong bathochromic shifts along this series.

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CAS Registry numbers:
(1), 57674-78-9; *(2)*, 57674-79-0; *(3)*, 57674-80-3; *(4)*, 57674-81-3; *(5)*, 57674-82-5

[1] A dodecafluorohexahydrotriscyclobuta[*a,c,e*]benzene has been claimed, but no structural proof was provided: *M. O. Riley* and *J. D. Park*, Tetrahedron Lett. *1971*, 2871.
[2] All new compounds gave satisfactory analytical and/or spectral data.
[3] *F. B. Mallory, C. S. Wood*, and *J. T. Gordon*, J. Am. Chem. Soc. *86*, 3094 (1964).
[4] *K. P. C. Vollhardt* and *R. G. Bergman*, J. Am. Chem. Soc. *96*, 4996 (1974).
[5] *R. H. Martin, N. Defay*, and *F. Geerts-Evrard*, Tetrahedron *20*, 1091 (1964).
[6] As shown by competition studies 4,5-diphenyl-1,2-dihydrocyclobutabenzene is not hydrogenated under these conditions.
[7] The degree of bond fixation may be larger than indicated by NMR chemical shifts since hybridization [8] and ring current effects (*e.g.* relative size of the ring currents of triphenylene, phenanthrene, benzene) may induce opposing trends.
[8] See *e.g. A. Streitwieser, G. R. Ziegler, P. C. Mowery, A. Lewis*, and *R. G. Lawler*, J. Am. Chem. Soc. *90*, 1357 (1968).
[9] *S. Friedman, S. Metlin, A. Svedi*, and *I. Wender*, J. Org. Chem. *24*, 1287 (1959); *J. J. Ward, W. R. Kirner*, and *H. C. Howard*, J. Am. Chem. Soc. *67*, 246 (1945); *S. Friedman, M. L. Kaufman*, and *I. Wender*, J. Org. Chem. *36*, 694 (1971).

Degenerate Butadienylcyclopropane Rearrangement in Tricyclo[5.3.0.0^{2,10}]deca-3,5-diene

By *Klaus Heger* and *Wolfram Grimme*[*]

We were recently able to show that above 110 °C bicyclo[5.1.0]octa-2,4-diene *(1)* undergoes degenerate butadienyl-

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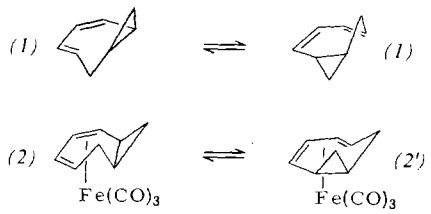
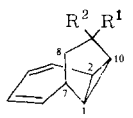
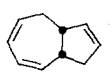
cyclopropane rearrangement; of the two quantum mechanically "allowed" transition states having cisoid or transoid conformation only the latter is involved[1]. However, the tricarbonyliron complex *(2)* having a fixed cisoid conformation formally undergoes the same rearrangement already at 90 °C[2]. The metal apparently lowers the activation barrier for the geometrically less favorable process.

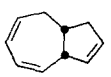


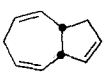
We here report the butadienylcyclopropane rearrangement in tricyclo[5.3.0.0^{2,10}]deca-3,5-diene *(3a)* whose cisoid geometry is fixed by the ethano bridge; no metal is involved in this rearrangement. On treatment with thionyl chloride and tri-*n*-butylamine in ether, tricyclo[5.3.0.0^{2,10}]deca-3,5-dien-9-ol *(3b)*[3] affords the chloride *(3c)*, which is reduced directly by lithium tetrahydridoaluminate in boiling tetrahydrofuran without further purification. Gas chromatography of the resulting hydrocarbon mixture (3 m, 20% Reoplex on kieselguhr, 45 ml He/min, 120 °C) affords *(3a)* [17% based on *(3b)*, retention time 7 min; NMR ($CDCl_3$, TMS internal): $\tau = 3.8$ (m) (2 olefinic H), 4.2 (m) (2 olefinic H), 6.9 (m) (7-H), 7.7—9.0 (m) (7 aliphatic H); UV (dioxane): $\lambda_{max} = 267$ nm ($\varepsilon = 4100$)] alongside the tetrahydroazulenes *(4)*, *(5)*, and *(6)*, probably formed by rearrangement of the chloride *(3c)*.



(3a), R^1 = H, R^2 = H
(3b), R^1 = H, R^2 = OH
(3c), R^1 = H, R^2 = Cl
(3d), R^1–R^2 = O
(3e), R^1 = H, R^2 = O_2C–C_6H_4–CO_2H
(3f), R^1 = H, R^2 = O_2C–C_6H_4–$CO_2^{\ominus}$ (+)–$H_3\overset{\oplus}{N}$–CH(CH_3)–C_6H_5


(4)


(5)


(6)

(3a) is stable up to 250 °C in the gas phase—the degenerate rearrangement is not manifested by this compound—and undergoes uniform rearrangement to *(6)* at higher temperature. A homopentadienyl hydrogen shift of the *endo* 9-H rationalizes this process.

Detection of the butadienylcyclopropane rearrangement was accomplished with the labeled compound [D_5]-*(3a)* (the heavily drawn positions are deuterated) prepared in conventional manner: on H/D exchange of 2,4,6-cycloheptatrien-1-ylmethyl diazomethyl ketone[3] in [OD]-ethanol (20 °C, pH 9) the diazomethyl position is labeled; this site becomes position 10 in [D_5]-*(3a)*. Using the same technique (20 °C, pH 14) the two α-methylene protons (8-H) are replaced in *(3d)*. Use of $LiAlD_4$ in the subsequent stepwise reduction of the ketone [D_3]-*(3d)* leads to [D_5]-*(3a)* [NMR ($CDCl_3$, TMS internal): olefinic H as in *(3a)*, $\tau = 6.92$ (t) (7-H), 8.4 (m) (1-H), 8.8 ppm (m) (2-H)[4]. Above 200 °C [D_5]-*(3a)* undergoes butadienylcyclopropane rearrangement in the gas phase to give its labeling isomer [D_5]-*(3'a)* with which it equilibrates [NMR ($CDCl_3$, TMS internal): olefinic H as in *(3a)*, $\tau = 6.92$ (broadened t) (0.5 7-H), 8.4 (m) (1-H), 8.8 ppm (m) (2-H and 0.5 10-H)[4]].

The rearrangement established for [D_5]-*(3a)* by isotopic labeling converts *(3a)* into its mirror image *(3'a)*. Because of the rather unproductive route to *(3a)* we have determined the kinetics of the rearrangement by polarimetry: *(3b)* is converted into the half-ester *(3e)* (40%, m.p. 117—119 °C) by treatment with phthalic anhydride in pyridine; reaction of *(3e)* with (+)-α-phenylethylamine in ethanol/hexane (1:1) gives the salt *(3f)* (79%, m.p. 132—135 °C). After four recrystallizations from ethanol/hexane (1:1) a fraction of constant melting point (46%, m.p. 141—142 °C) is obtained, whose cleavage with 5% hydrochloric acid furnishes the half-ester (−)-*(3e)*[5] (75%, m.p. 119—121 °C). Reduction with $LiAlH_4$ in ether gives the alcohol (−)-*(3b)* [97%, $[\alpha]_D^{20} = -34.5°$ (in $CHCl_3$)] which is transformed into the chloride and reduced as described above. Gas chromatography of the product mixture yields (−)-*(3a)* [14%, $[\alpha]_D^{25} = -10.0°$, $[\alpha]_{407.7}^{20} = -19.5°$ (both in *n*-dodecane)].

Racemization of (−)-*(3a)* was followed up to a loss of at least 60% of rotatory power in 0.1 M dodecane solution at four temperatures between 179 and 193 °C. Tetralin was added as an internal standard to the degassed samples which were then sealed into glass ampoules; each polarimetric measurement ($\lambda = 407.7$ nm) was accompanied by a gas chromatographic loss analysis[6]. The racemization follows first order kinetics, and the temperature dependence of its rate constant is reproduced by the Arrhenius equation

$$\log k = (13.53 \pm 0.2) - (37\,800 \pm 300)/2.303\,RT$$

The free energy of activation of the butadienylcyclopropane rearrangement in *(3a)* is thus about 5.0 kcal/mol higher than that in *(1)*[1]. Bearing in mind that *(1)* must first be transformed into its higher energy transoid conformer, the energy difference for the pericyclic reaction itself in the cisoid as against the transoid transition state should be taken as $\Delta\Delta F^{\neq} \geq 6$ kcal/mol. It remains to be established whether this difference is overcome also in the case of *(3a)* by coordination to the $Fe(CO)_3$ group.

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CAS Registry numbers:
(±)-*(3a)*, 57674-70-1; (−)-*(3a)*, 57674-71-2; (±)-*(3b)*, 57674-72-3; (−)-*(3b)*, 57674-73-4; (±)-*(3c)*, 57674-74-5; *(3d)*, 15719-07-0; (±)-*(3e)*, 57674-75-6; (−)-*(3e)*, 57674-76-7; *(3f)*, 57759-53-2; *(4)*, 57674-77-8; *(5)*, 57739-04-5

[1] *W. Grimme* and *W. von E. Doering*, Chem. Ber. *106*, 1765 (1973).
[2] *R. Aumann*, Angew. Chem. *85*, 628 (1973); Angew. Chem. Int. Ed. Engl. *12*, 574 (1973).
[3] *W. von E. Doering, B. M. Ferrier, E. T. Fossel, J. H. Hartenstein, M. Jones, Jr., G. Klumpp, R. M. Rubin*, and *M. Saunders*, Tetrahedron *23*, 3943 (1967).
[4] Assignment of the signals corresponds to that established by double resonance for [D_2]-*(3d)* [1].
[5] The absolute configuration of (−)-*(3e)* and its reaction products is unknown; the enantiomeric configuration *(3')* is just as likely.
[6] Losses never exceeded 10%.

Chlorine Isotope Effects in Ion Exchange Chromatography[**]

By *Klaus G. Heumann* and *Rainer Hoffmann*[*]

Isotope effects on ion exchange equilibria with metal cations have already been repeatedly investigated[1-3]. However, only few studies have been performed on anions; for instance, there is only one relevant publication for chloride which gives no precise details about variations in the isotope effect[4]. In order to gain a better insight into isotope effects in anion exchange equilibria, on the one hand, and to test the possibilities of chromatographic chlorine isotope enrichment, on the other, we have undertaken relevant studies on ion exchange columns.

All experiments were performed in a column (height of packing, 80 cm; column diameter, 1.5 cm) packed with the strongly basic anion exchanger AG1-X10 (NO_3^- form, 200 to 400 mesh, Bio-Rad) at 20 °C. In each run, 200 mg samples of chloride of natural isotope abundance were applied to the column as NaCl and eluted with 0.01, 0.1, or 1 M $NaNO_3$ solution. The elution rate was 0.35—0.40 ml/min. The eluate was collected in fractions and the isotope ratio $^{35}Cl/^{37}Cl$ was determined by thermionic mass spectrometry in several of these fractions.

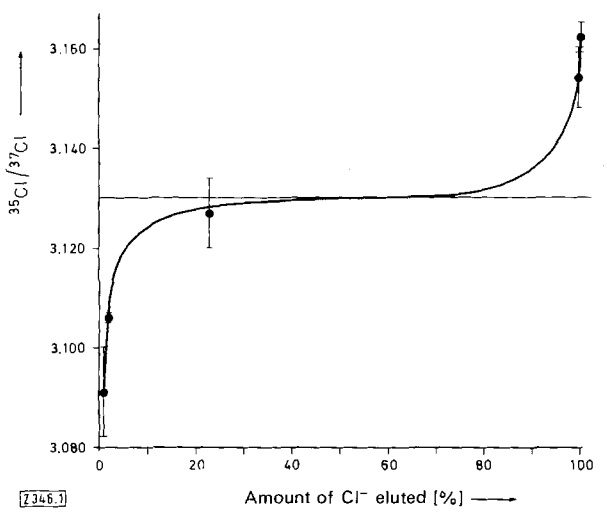

Fig. 1. Isotope ratio $^{35}Cl/^{37}Cl$ as a function of the amount of Cl^- eluted. Eluant: 0.1 M $NaNO_3$. The horizontal line indicates the starting isotope ratio $^{35}Cl/^{37}Cl = 3.130$.

At all concentrations of eluant we found an enrichment of the heavy isotope ^{37}Cl in the first fractions and a depletion of this isotope in the last fractions (see Fig. 1). The differential selectivity of $^{35}Cl^-$ and $^{37}Cl^-$ accords with the results obtained in studies of isotope effects of metals on cation exchangers[1, 3]. This enrichment can be attributed to the slightly greater ionic radius of the lighter metal isotope[1, 5]. Application of this explanation to the Cl^- isotopes would require $^{35}Cl^-$ to have a somewhat larger ionic radius than $^{37}Cl^-$. This assumption is in accord with the ionic radius differences calculated for pairs of halogen isotopes[6]. In a steady state experiment it could be shown that the chlorine isotope effect in the column experiments was not kinetic in origin: after equilibration the same enrichment tendency was observed.

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With the aid of a computational method due to *Glueckauf*[7] we have been able to perform the first calculation of the elementary separation factor $\alpha = 1 + \varepsilon$ of one equilibrium stage corresponding to the isotope exchange equilibrium eq. (1) from the results of column chromatography (soln = solution, ex = exchanger):

$$^{35}Cl^-_{soln} + {}^{37}Cl^-_{ex} \rightleftharpoons {}^{35}Cl^-_{ex} + {}^{37}Cl^-_{soln} \quad (1)$$

The elementary isotope effect decreases with increasing concentration of the $NaNO_3$ solution used as eluant (concentration: 0.01, 0.1, and 1.0 mol/l; $\varepsilon = 5.4 \times 10^{-4}$, 3.0×10^{-4}, and 1.9×10^{-4} respectively). This accords with observations made during analogous experiments with lithium isotopes[8]. The results can be explained in terms of the theory of concentrated electrolytes in relation to ion exchange resins[9]. The variation of the isotope effect with the eluant concentration is attributed to differential modification of the activity coefficients of the isotopes in the ion exchanger phase and in the aqueous phase.

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German version: Angew. Chem. 88, 54 (1976)

CAS Registry numbers:
$^{35}Cl^-$, 32997-85-6; $^{37}Cl^-$, 42150-36-7

[1] *E. Glueckauf*, J. Am. Chem. Soc. *81*, 5262 (1959).
[2] *G. Dickel* and *K. Richter*, Z. Naturforsch. *19a*, 111 (1964).
[3] *K. G. Heumann* and *K. H. Lieser*, Z. Naturforsch. *27b*, 126 (1972).
[4] *T. Langvad*, Acta Chem. Scand. *8*, 526 (1954).
[5] *K. G. Heumann*, *R. Hoffmann*, and *W. Luecke*, Z. Naturforsch. *30b*, 497 (1975).
[6] *D. N. Knyazev*, Russ. J. Phys. Chem. *35*, 298 (1961).
[7] *E. Glueckauf*, Trans. Faraday Soc. *54*, 1203 (1958).
[8] *D. A. Lee* and *J. S. Drury*, J. Inorg. Nucl. Chem. *27*, 1405 (1965).
[9] *D. C. Whitney* and *R. M. Diamond*, Inorg. Chem. *2*, 1284 (1963).

Electrophilic Alkylation-Cycloaddition between an Olefinic and an Acetylenic Substrate

By *Karl Griesbaum* and *Wolfgang Seiter*[*]

In order to assess the synthetic possibilities which may arise from cationically induced crossover reactions between olefinic and acetylenic substrates, we are investigating reactions of hydrogen halides with mixtures of olefinic and acetylenic substrates.

In the reaction of anhydrous hydrogen chloride with propene and propyne (molar ratio of 2:1:1, respectively) in the liquid phase, the crossover products *(3)*—*(6)* were obtained, in addition to the products which are formed in the individual reactions of HCl with propene and with propyne, respectively[1]. The crossover products *(3)*—*(6)* have been isolated as colorless liquids by means of preparative gas chromatography (5% Nitrilesilicon oil on Chromosorb G). The previously known compounds *(3)*, *(4)* and *(5)* were identified by NMR and IR spectroscopy. The proposed structure of *(6)* is supported by its elemental analysis, its mass spectrum (M^+ at *m/e* 198, 196, 194) and its 100-MHz ^1H-NMR spectrum (CCl_4): $\delta = 0.93$ (d, isopropyl-CH_3), 1.02 (d, isopropyl-CH_3, $J = 6$ Hz), 1.75 (s, CH_3), 1.85 (s, CH_3), 2.38 (d, 2-H, $J = 10.5$ Hz), AB quartet at $\delta_A = 2.62$, $\delta_B = 2.70$ (2 4-H, $J = 13.5$ Hz), $\delta = 2.07$ (m, isopropyl-H).

Apparently, the crossover products *(3)*—*(6)* are the result of an alkylation of propyne with the isopropyl cation *(1)*. Their formation can be readily rationalized by the intermediacy of the vinyl cation *(2)*. The formation of the trialkyl

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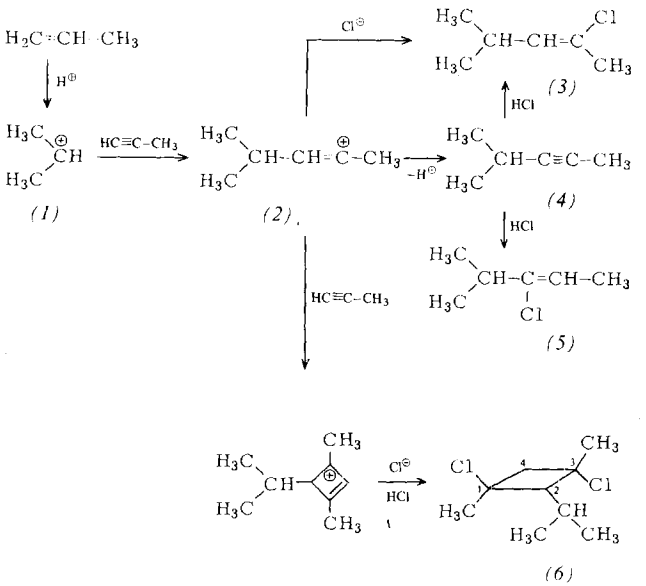

substituted dichlorocyclobutane *(6)* can thus be considered as an alkylation-cycloaddition between one molecule of propene, two molecules of propyne and HCl. It is a modification of cycloadditions *via* vinyl cations as intermediates[1, 2] and, as an alternative to the simple [2+2]-cycloadditions, it opens up new possibilities for the one-step synthesis of substituted cyclobutanes.

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German version: Angew. Chem. *88*, 57 (1976)

[1] The major products from the reaction of non-aqueous hydrogen chloride with propyne have been reported by us previously: *K. Griesbaum* and *M. El Abed*, Chem. Ber. *106*, 2001 (1973).

[2] *J. H. Lukas, A. P. Kouwenhoven*, and *F. Baardman*, Angew. Chem. *87*, 740 (1975); Angew. Chem. Int. Ed. Engl. *14*, 709 (1975).

1,3-Diarsacyclobutanes

By *Hans-Jürgen Padberg* and *Günter Bergerhoff*[*]

Whereas arylphosphorus dichlorides eliminate HCl to give 1,2-diphosphacyclopentenes on treatment with malonic esters[1], alkyl- and arylarsenic dichlorides afford 1,3-dialkyl- and 1,3-diaryl-1,3-diarsacyclobutanes *(1)* under the same conditions (Table 1). Hitherto only 1,2-diarsacyclobutene has received brief mention[2].

(1b) crystallizes from benzene as colorless polyhedra and only decomposes above 200 °C. Moreover, it is readily soluble in dichloromethane, chloroform, and tetrahydrofuran, less so in ethanol and ether, and not at all in water, even when hot. On exposure to air the crystals are subject to only insignificant decomposition within several weeks. *(1b)* reacts with equimolar amounts of anhydrous HI or halogen to give $PhAsI_2$, an excess of HI affords AsI_3[3].

The structure of *(1b)* is confirmed by quantitative elimination of HCl during its synthesis and by the results of elemental analysis and cryoscopic molecular weight determination. The mass spectrum contains, *inter alia*, peaks for M^+ (620, 65%) and $(M/2)^+$ (310, 100%). The IR spectrum displays As—Ph absorptions (*e.g.* at 698 and 470 cm^{-1} [4]) and a single C=O absorption at 1710 cm^{-1}, indicating the equivalence of the four ester groups. In analogy to P compounds the absorptions in the range 790—880 cm^{-1} can be interpreted as As—C—As vibrations[5]; however, absorptions typical of As—As compounds are absent[6]. (For the ^{1}H-NMR spectrum, see Table 1.)

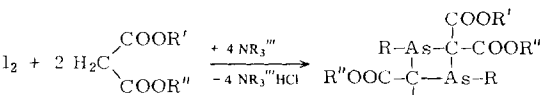

Table 1. Diarsacyclobutanes *(1)* prepared.

(1)	R	R′=R″	^{1}H-NMR [a] H in R	H in R′	M.p. [°C]	Yield [%]
a	C_6H_5	CH_3	7.28—7.78	3.33 (s)	168	55
b	C_6H_5	C_2H_5	7.20—7.75	0.85 (t), 3.73 (m) [b]	145	40
c	C_6H_5	$C(CH_3)_3$				[c]
d	CH_3	CH_3	1.27 (s)	3.72 (s)	176	75
e	CH_3	C_2H_5	1.30 (s)	1.27 (t), 4.26 (q)	102	60
f	CH_3	$C(CH_3)_3$	1.32 (s)	1.46 (s)	208	10
g [d]	CH_3	C_2H_5	1.30 (s)	1.26 (t), 4.20 (m)	162	35
h	$C(CH_3)_3$	$C(CH_3)_3$				[c]

[a] δ values, recorded in $CDCl_3$ at 37 °C, TMS internal standard.
[b] The methylene protons give a duodecet; $\delta_A = 3.59$, $\delta_B = 3.88$, $J_{AB} = 11$ Hz.
[c] In this case the greater bulk of the *tert*-butyl groups apparently leads only to linear products which are still being investigated.
[d] In *(1g)* R′≠R″; R′=C_2H_5, R″=$C(CH_3)_3$; ^{1}H-NMR (H in R″): δ = 1.44 (s).

Fig. 1. Stereo pair of tetraethyl 1,3-diphenyl-1,3-diarsa-2,2,4,4-cyclobutanetetracarboxylate *(1b)*.

As shown in Figure 1, the benzene rings are oriented such that the free rotation of the ester groups is restricted owing to the bonding angle of about 90° at the As atom. The molecule possesses only a two-fold axis and is chiral. The steric hindrance is alleviated on replacement of the phenyl by a methyl group as in *(1e)* and the expected quartet splitting of the CH_2 is then observed.

Tetraethyl 1,3-diphenyl-1,3-diarsa-2,2,4,4-cyclobutanetetracarboxylate (1b)

To a stirred solution of diethyl malonate (5 g, 31 mmol) and triethylamine (6.3 g, 62 mmol) in benzene (125 ml) at room temperature is added dropwise within 2–3 h a solution of phenylarsenic dichloride (6.95 g, 31 mmol) in benzene (50 ml). After 12 h about 90% of the ammonium salt has precipitated and is filtered off. Evaporation of the solvent leaves a faintly yellow substance which is washed with ether/light petroleum and can be recrystallized from benzene/ether.—Compounds *(1a)* and *(1d)*—*(1g)* are prepared in analogous fashion, but preferably washed with methanol/ether.

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CAS Registry numbers:
(1a), 57694-84-5; *(1b)*, 57694-85-6; *(1d)*, 57694-86-7; *(1e)*, 57694-87-8; *(1h)*, 57694-88-9; *(1g)*, 57694-89-0;

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Anorganisch-chemisches Institut der Universität
53 Bonn, Max-Planck-Strasse 1 (Germany)

$C_6H_5AsCl_2$, 696-28-6; CH_3AsCl_2, 593-89-5; $(CH_3)_3CAsCl_2$, 4262-41-3; $H_2C(COOCH_3)_2$, 108-59-8; $H_2C(COOC_2H_5)_2$, 105-53-3; $H_2C(COOC(CH_3)_3)_2$, 541-16-2; $H_2C(COOC_2H_5)(COOC(CH_3)_3)$, 32864-38-3

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ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

The chemistry of electronically excited states of coordination compounds is reviewed by *V. Balzani, L. Moggi, M. F. Manfrin, F. Bolletta*, and *G. S. Laurence*. Recent data on sensitization and quenching of photochemical reactions and luminescence of coordination compounds are collected. The kinetics and mechanisms of formation and deactivation of excited states are discussed, and examples for applications in coordination chemistry are given, *e.g.* identification of photoreactive states, increasing of quantum yields, and extension of the photochemically useful spectral range by sensitization. [Quenching and Sensitization Processes of Coordination Compounds. Coord. Chem. Rev. *15*, 321—433; 216 references]

[Rd 806 IE—H]

Biosynthesis and secretion of insulin forms the theme of a review by *M. A. Permutt* and *D. M. Kipnis*. A glucose receptor system of the cell membrane is obviously responsible for the stimulation of insulin secretion by glucose. This stimulation takes place both at the transcription level and thereafter. Phoridzin, a glucoside with high affinity for the glucose carrier system of plasma membranes, strongly stimulates the secretion of insulin; of the many plant lectins that have been studied only one mushroom lectin displayed a stimulating action. The part of the stimulation occurring after transcription is due to an augmented initiation of mRNA. Proinsulin is synthesized in polysomes carrying six to eight ribosomes. The proinsulin mRNA is thus surprisingly long. [Insulin Biosynthesis and Secretion. Fed. Proc. *34*, 1549—1555 (1975); 23 references]

[Rd 812 IE—R]

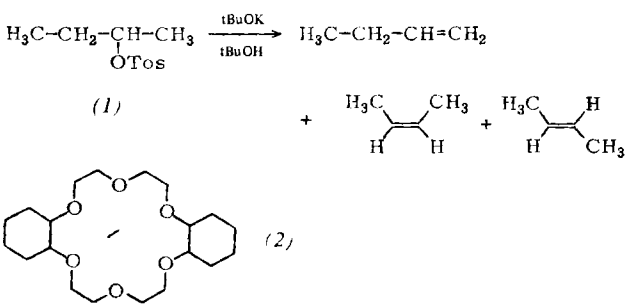
Interaction of insulin with membrane receptors and its relationship to cyclic purine nucleotides and cell growth are reviewed in an article by *M. D. Hollenberg* and *P. Cuatrecasas*. The insulin receptor of fat and liver cells is a large glycoprotein with high insulin-affinity and -specificity; other membrane components also take part in the binding. In order to explain the relationship between insulin and the cyclic nucleotides it is hypothesized that a single cyclase produces both cAMP as well as cGMP, depending on the type of hormonal stimulation. The article also deals with the relationship between insulin action and membrane phosphorylation, influences on cAMP and cGMP levels, on growth, on DNA synthesis, and on the uptake of α-aminoisobutyric acid in fibroblasts—processes which, in part, only take place at unphysiologically high concentrations of insulin. [Insulin: Interaction with Membrane Receptors and Relationship to Cyclic Purine Nucleotides and Cell Growth. Fed. Proc. *34*, 1556—1563 (1975); 99 references]

[Rd 813 IE—R]

The catalytic function of hydrogen which is bound to oxide surfaces is surveyed by *W. K. Hall*. Depending upon the oxide (*e.g.* aluminosilicates, zeolites, alumina, zinc oxide) and the reaction conditions, the hydroxyl groups located on the surface can act as Brønsted acids, or the catalytic activity originates from strongly polar centers arising by loss of water on heating. The reactions and phenomena discussed include the formation of carbenium ions, chemisorption, olefin isomerization, D/H exchange in hydrocarbons, and H_2/D_2 exchange and allotropic conversions. [Catalytic Function of Hydrogen Bound to the Surfaces of Oxides. Acc. Chem. Res. *8*, 257—263 (1975); 48 references]

[Rd 815 IE—L]

Association of ions in base-promoted β-eliminations is reviewed by *R. A. Bartsch*. The β-elimination reaction of the tosylate *(1)* may be cited as example. While *cis*- and *trans*-2-butene are formed in the ratio 1:0.4 with potassium *tert*-butoxide



in *tert*-butyl alcohol at 50 °C, the *trans* isomer predominates (*cis*:*trans* = 1:1.9) on addition of the crown ether *(2)*. This result can be interpreted in terms of complexation of the potassium ion by the crown ether, which considerably reduces the association of the potassium *tert*-butoxide

$$n\,tBuO^{\ominus}\,n\,K^{\oplus} \rightleftharpoons n(tBuO^{\ominus}K^{\oplus}) \rightleftharpoons (tBuO^{\ominus}K^{\oplus})_n$$

There are numerous examples illustrating the influence of ionic association on orientation and stereochemistry in β-eliminations of this kind; alkene synthesis should be facilitated by the use of crown ethers. [Ionic Association in Base-Promoted β-Elimination Reactions. Acc. Chem. Res. *8*, 239—245 (1975); 65 references]

[Rd 817 IE—L]

The structure and properties of collagen and its characterization in the solid state are considered in a review by *J. C. W. Chien*. Some 20—30% of the protein present in vertebrates is in the form of collagen; its concentration is particularly high in skin, sinews, and bones. Apart from the primary to quaternary structure, macroscopic ultrastructures made up of ordered aggregates also have to be considered in collagen. Collagen is semicrystalline. A section each is devoted to application of the two-phase model, mechanical and dielectric properties, denaturation, and biomedical applications. [Solid-State Characterization of the Structure and Properties of Collagen. Rev. Macromol. Chem. *13*, 1—80 (1975); 252 references]

[Rd 818—IE L]

The coupling of "high-energy" phosphate bonds to energy transductions is reviewed in an article by *P. D. Boyer, B. O. Stokes, R. G. Wolcott*, and *C. Degani*. According to recent opinion it would appear that the primary function of the energy in oxidative phosphorylation lies in the liberation of ATP, which is formed on reversal of hydrolysis. The authors suggest that the conformational changes observed on ATP binding and cleavage play an essential role in the function of the mitochondria and also in other ATP-dependent processes, such as muscle contraction. [Coupling of "High-Energy" Phosphate Bonds to Energy Transductions. Fed. Proc. *34*, 1711—1717 (1975); 46 references]

[Rd 810 IE—R]

BOOK REVIEWS

Die Analyse der Luft und ihre Verunreinigungen in der freien Atmosphäre und am Arbeitsplatz (Analysis of Air and its Impurities in the Free Atmosphere and at Places of Work). By *W. Leithe*. Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart 1974. 2nd revised and expanded edition, xv, 303 pp., 49 figs., bound, DM 74.—.

A second edition of *Leithe*'s book has now appeared, only a few years after publication of the first. Again we have an essentially practical book providing valuable assistance to the ever-increasing number of users of methods of air analysis. This should be particularly emphasized, because there is in the German language no other presentation of the theme in a monograph that, like the present conveniently handleable volume, is comprehensive, accurate, and topical.

In his subdivision of the subject the author proceeds rigorously from the general to the specialized. First, in a general section, he provides the reader with conceptual and historical basic information, then reports briefly on the legal requirements, measures, and procedures for technological management in various countries as regards purification of the air and labor protection. He follows this up with bibliographic references, and then goes into the sources of atmospheric impurities and the form in which they appear, into the technology of reducing their emission, into the distribution of foreign materials, and into their importance in hygiene, while paying particular attention to limiting values and their definition.

The second main section provides in concentrated form the tools needed for air analysis in industrial practice. Here are discussed the quantitative aspects of the analyses, the purposes of the investigations, and the choice of measuring procedures and the analysis level in special cases, *e.g.* the determination of background impurities. The methods and problems of sampling and of sample enrichment are discussed in detail. The preparation and the use of reference gas mixtures are treated with remarkable topicality in accord with the importance of calibration and of investigation of their effects.

There follows a special methodological section in which, along with test-tube processes, are treated above all and with examples, the instrumental methods relying on the application of spectrochemical, electrochemical, and chromatographic principles, as well as the analytical use of the sense of smell. In view of the rapidity of technical developments, it is not surprising that some of the processes described have meanwhile been abandoned, *e.g.* reversion chromatography. It will not be considered a shortcoming that the author has rejected discussion of remote-measurement methods whose validity is still disputed, *e.g.* Lidar and correlation spectrometry.

More than half of the book is taken up by the specialized part. This part provides analytical methods for air contaminated with a wide variety of inorganic or organic constituents, these methods all being of the nature of complete analytical prescriptions by means of which the work can be carried out without the need to allow for considerable unsuspected difficulties. These prescriptions are enhanced by a wealth of literature references reaching to around 1972; newer developments are thus included, such as the application of chemiluminescence analysis to the determination of ozone and nitrogen oxides. The book ends with tables giving conversion factors, material constants, and limiting values. Taken as a whole, the volume is presented in a pleasant, technically sound, and solid manner, and its few irregularities will surely be corrected at a later date.

Heinrich Hartkamp [NB 286 IE]

Progress in Mass Spectrometry. Fortschritte der Massenspektrometrie. Edited by *H. Budzikiewicz*. **Vol. 1. Indolalkaloide** (Indole Alkaloids). Part 1: Text, Part 2: Spektren (Spectra). By *M. Hesse*. Verlag Chemie, GmbH, Weinheim 1974. 1st Edit., Part 1: xvii, 261 pp., 95 schemes, 42 tables; Part 2: vii, 98 pp., 173 spectra; linen-bound, together DM 98.—. **Vol. 2: Chroman and Related Compounds.** By *S. E. Drewes*. Verlag Chemie, GmbH, Weinheim 1974. 1st Edit., vii, 138 pp., 33 figs., 102 schemes, linen-bound, DM 58.—.

Today it is difficult even for the expert to survey the relationships between structure and mass spectra of a certain class of compounds, because the literature is widely scattered and some of the important data are hidden in the experimental parts of papers. The present series of monographs therefore meets a true need and will provide much saving in literature searches.

In the first volume *Hesse*, who is probably the leading expert on indole alkaloids, gives an exhaustive review of this special field. In the first part the characteristic decomposition reactions of the individual types of compounds are arranged in subgroups and critically discussed, while the second part contains all the relevant spectral data. The most important data and references can be derived from tables at the beginning of each section. The two volumes can serve as models of their kind and will prove invaluable to all who are active in this field.

The second volume, which is compiled by *Drewes* and concerns the mass spectra of chromans and related compounds, is in the reviewer's opinion less successful. For example, the formulas do not contain the numbering of the often complex compounds, which is necessary for rapid under-

standing (in the first volume each compound is numbered throughout), and the formulas are often found only one or two pages before or after they have been mentioned in the text. What is more troublesome is that the author has not always made happy choices and, for example, formulates diradical ions that, for energetic reasons, are certainly not formed (*e.g.* on pp. 74 and 75 the ion with mass 135), although admittedly the ions postulated are useless as criteria since they often have only a low intensity (on p. 76, 3 %). Nevertheless, the author has collected the literature concerning chromans, xanthones, and flavanoids with great diligence, so that the critical reader has a book that will greatly assist him in working his way into the mass spectrometry of this class of compounds.

Gerhard Spiteller [NB 284 IE]

Serumproteine. Bd. 1: Methodische Fortschritte im medizinischen Laboratorium [Serum Proteins. Vol. 1. Progress in Medical Laboratory Techniques]. Edited by *A. Englhardt* and *H. Lommel*. Verlag Chemie GmbH, Weinheim 1974. 1st Edit., 230 pp., 67 figs., 40 tables, bound, DM 52.—.

This books, published in 1974, provides a collection of articles on the qualitative and quantitative analysis of serum proteins. There is no review giving a critical evaluation of the now available methods of clinical diagnosis. The reader must make do with the individual chapters, which are of very varied quality. In some chapters (*e.g.* in the introductory chapter by *A. Englhardt*) the emphasis is on the experimental methods, the main weight being laid on their interpretation. In Chapter II (Special Proteins) there appears to be some lack of coordination, since the explanation and the interpretation of the same methods are repeated in several different contributions. While the schemes are mostly very well drawn, the reproduction of the original diagrams is so bad that it is often barely possible to recognize the essential features. Unfortunately, also, the collection of methods is incomplete, in that newer techniques such as *Laurell*'s "rocket" electrophoresis and the "automatic" techniques for quantitative analysis of plasma proteins are not included. Instead, we have a modification of immunoelectrophoresis by *R. Sanders* and *H. G. Meiers* that is no longer used in general practice. The chapters dealing with immunoelectrophoresis and its interpretation suffer particularly badly from the poor quality of the diagrams in this chapter; however, the experimental instructions are given in detail sufficient to enable the newcomer to use the methods described. Overlapping occurs also in Chapter IV (Lipoproteins), and in Chapter V (Enzymes and Isoenzymes). Chapter VI (Antibodies) contains contributions on experimental methods that are in the main clearly written, critical, and complete, although here too there is some overlap. The tables in the article on "Detection of Australia SH Antigens and Antibodies" contain mainly the older, insensitive methods such as transport electrophoresis, the Mancini technique, and the complement-fixation reaction which are today replaced by more sensitive methods (mentioned only as literature references). In the chapter on the detection of the various autoantibodies the critical evaluation of the methods is incomplete. Where immunofluorescence methods are applied there is no precise description of the microscopic techniques. The book closes with an excellent chapter on the detection and evaluation of antibodies in the thyroid gland.

It is hoped that in future volumes of the series the publishers will see to it that the quality of the printing is improved and that there is thorough in-house editing.

H. Deicher [NB 289 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Verordnung über gefährliche Arbeitsstoffe. (Directive on hazardous working materials.) Textausgabe mit Einführung, ausführlichen Erläuterungen für die Praxis und Formularabbildungen. (Text with introduction, detailed practical notes, and facsimiles of forms and specifications.) WEKA-Verlag Fachverlag für Verwaltung und Industrie, Kissing 1975. 225 pp., stitched, DM 36.—.

Polymer-Plastics Technology and Engineering, Vol. 4. Edited by *L. Naturman*. Marcel Dekker, New York 1975. xi, 249 pp., bound, $ 32.50.

Hypothalamic Hormones—Structure, Synthesis and Biological Activity. Edited by *D. Gupta* and *W. Voelter*. Verlag Chemie, Weinheim 1975. 318 pp., bound, DM 58.—.—Proceedings of the European Colloquium on Hypothalamic Hormones held at Tübingen in February 1974.

Allgemeine Chemie. Energetik, Dynamik und Struktur chemischer Systeme. By *J. A. Campbell*. Verlag Chemie, Weinheim 1975. ivxx, 1223 pp., bound, DM 78.—.

BAG Chemie-Lexikon. By *H. P. Stauffer* and *U. von Arx*. Band A: Geräte, Zubehör und Einrichtungen für die Verfahrenstechnik. Band B: Geräte, Zubehör und Einrichtungen für die Laboratoriumstechnik. BAG Brunner Verlag AG, Zürich/Verlag Chemie, Weinheim 1975. Band A: 344 pp. Band B: 400 pp., bound, each DM 115.—.

Umwelt und Chemie von A—Z. A contribution to environmental problems. Issued by the Verband der Chemischen Industrie. Verlag Herder, Freiburg 1975. 148 pp., paper. Obtainable free of charge from Verband der Chemischen Industrie.

Organic Compounds of Sulphur, Selenium, and Tellurium, Vol. 3. Senior Reporter: *D. H. Reid*. The Chemical Society, London 1975. xxv, 805 pp., bound, 25.00.—A volume in the series "Specialist Periodical Reports".

Thermodynamics of Fluids. An Introduction to Equilibrium Theory. By *K. C. Chao* and *R. A. Greenkorn*. Vol. 4 of the series "Chemical Processing and Engineering". Edited by *L. F. Albright, R. N. Maddox*, and *J. J. McKetta*. Marcel Dekker, New York 1975. xi, 553 pp., bound, $ 29.75.

Propellanes. Structure and Reactions. By *D. Ginsburg*. Vol. 7 of the series "Monographs in Modern Chemistry". Edited by *H. F. Ebel*. Verlag Chemie, Weinheim 1975. 272 pp., bound, DM 138.—.

Deutsche Einheitsverfahren zur Wasser-, Abwasser- und Schlammuntersuchung. Physical, chemical, biological, and bacteriological methods. Issued by the Fachgruppe Wasserchemie in der Gesellschaft Deutscher Chemiker. 7th instalment (1975 delivery). Verlag Chemie, Weinheim. 3rd completely new and revised edition, loose-leaf instalment, DM 33.—.

Biochemie. By *A. L. Lehninger*. Verlag Chemie, Weinheim 1975. xv, 747 pp., bound, DM 78.—, paper, DM 68.—.

Fortran IV in Chemistry. An Introduction to Computer-assisted Methods. By *G. Beech*. John Wiley & Sons, London 1975. x, 303 pp., bound, £ 8.75.

Miltitzer Berichte über Ätherische Öle, Riechstoffe usw. Ausgabe 1973. Issued by the Chemisches Kombinat Miltitz. 206 pp., paper.

Determination of Uranium and Plutonium in Nuclear Fuels. By *H. Sorantin*. Vol. 5 of the series "Kernchemie in Einzeldarstellungen". Edited by *K. H. Lieser*. Verlag Chemie, Weinheim 1975. viii, 285 pp., bound, DM 138.—.

Methods in Narcotics Research. Edited by *S. Ehrenpreis* and *A. Neidle*. Vol. 5 of the series "Modern Pharmacology-Toxicology". Edited by *W. F. Bousquet* and *R. F. Palmer*. Marcel Dekker, New York 1975. xi, 408 pp., bound, $ 29.75.

Radiochemie. By *C. Keller*. From the series "Studienbücher Chemie". Diesterweg-Salle, Frankfurt/Sauerländer, Aarau 1975. vi, 202 pp., paper, DM 12.80.

Molecular Structure by Diffraction Methods, Vol. 3. Senior Reporters: *G. A. Sim* and *L. E. Sutton*. The Chemical Society, London 1975. xiv, 514 pp., bound, £ 26.00.—A volume in the series "Specialist Periodical Reports".

Applied Spectroscopy Reviews, Vol. 9. Edited by *E. G. Brame, Jr.* Marcel Dekker, New York 1975. xiv, 321 pp., bound, $ 32.50.

Radioimmunoassay in Clinical Biochemistry. Edited by *C. A. Pasternak*. Heyden, London 1975. xvii, 299 pp., bound, £ 13.80.

Advances in Infrared and Raman Spectroscopy, Vol. 1. Edited by *R. J. H. Clark* and *R. E. Hester*. Heyden, London 1975. xiii, 306 pp., bound, £ 13.80.

Protein Nutritional Quality of Foods and Feeds. Part 2: Quality Factors—Plant Breeding, Composition, Processing, and Antinutrients. Edited by *M. Fiedman*. Vol. 1 of the series "Nutrition and Clinical Nutrition". Edited by *R. E. Olson*. Marcel Dekker, New York 1975. xx, 674 pp., bound, $ 49.50.

Röntgenbeugung an Kristallen. By *K.-H. Jost*. Akademie-Verlag, Berlin 1975. xii, 404 pp., bound, *ca.* DM 98.—.

The Physics of Time Asymmetry. Von *P. C. W. Davies*. Surrey University Press/Intertext Publishing Ltd., Guildford 1975. xviii, 214 pp., bound.

Reaktionstypen in der anorganischen Chemie. By *I. Fitz*. Akademie-Verlag, Berlin 1975. 465 pp., bound, *ca.* DM 58.—.

Coordination Polymerization. Edited by *J. C. W. Chien*. Academic Press, New York 1975. xii, 353 pp., bound, $ 16.00.

Physiologische Chemie. Eine Einführung in die medizinische Biochemie für Studierende der Medizin und Ärzte. By *H. Harper, G. Löffler, P. E. Petrides*, and *L. Weiss*. Springer-Verlag, Berlin 1975. xii, 940 pp., paper, DM 88.—.

Datensammlung Chemie in SI-Einheiten. By *G. H. Aylward* and *T. J. V. Findlay*. Volume 27 of the series "taschentext". Verlag Chemie, Weinheim 1975. x, 158 pp., paper, DM 14.80.

Chemistry and Biochemistry of Thiocyanic Acid and its Derivatives. Edited by *A. A. Newman*. Academic Press, New York 1975. xiv, 351 pp., bound, $ 29.75.

Integrierter naturwissenschaftlicher Unterricht in der Bundesrepublik Deutschland. By *K. Frey*. IPN-Kursbericht 2. Institut für die Pädagogik der Naturwissenschaften an der Universität Kiel. 31 pp., paper.

Farbenlehre und Farbenmessung. By *W. Schultze*. Springer-Verlag, Berlin 1975. 3rd revised edition, vii, 97 pp., paper, DM 32.—.

The Physics of Rubber Elasticity. By *L. R. Treloar*. From the series "Monographs on the Physics and Chemistry of Materials". Edited by *C. E. H. Bawn, H. Fröhlich, P. B. Hirsch*, and *N. F. Mott*. Clarendon Press, Oxford 1975. 3rd Edit., xii, 310 pp., bound, £ 14.00.

Petroleum Refining. Technology and Economics. By *J. H. Gary* and *G. E. Handwerk*. Vol. 5 of the series "Chemical Processing and Engineering". Edited by *L. F. Albright, R. N. Maddox*, and *J. J. McKetta*. Marcel Dekker, New York 1975. x, 365 pp., bound, $ 24.50.

Hochdruck-Flüssigkeits-Chromatographie. By *H. Engelhardt*. Band 14 of "Anleitungen für die chemische Laboratoriumspraxis". Edited by *F. L. Boschke*. Springer-Verlag, Berlin 1975. x, 213 pp., bound, DM 56.—.

Chemische Reaktionstechnik. By *K. Dialer* and *A. Löwe*. Carl Hanser Verlag, München 1975. 108 pp., paper, DM 22.—.

Einführung in die Physikalische Chemie. Teil II: Kinetik. By *H. Labhart*. From the series "Hochschultext". Springer-Verlag, Berlin 1975. x, 105 pp., paper, DM 13.60.

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Chemistry and Biochemistry of Unsaturated Fatty Acids

By Wolf-H. Kunau[*]

Although unsaturated fatty acids have long been known to accompany saturated fatty acids in most lipids, qualitative and quantitative determination of fatty acid patterns only became possible with the advent of modern analytical methods. Present day knowledge of the chemical structure, physical properties, and metabolism of unsaturated fatty acids provides the basis for the development of new concepts of their function. Thus unsaturated fatty acids crucially determine the properties of biological membranes. Moreover, essential fatty acids are precursors of prostaglandins.

1. Introduction

Fatty acids are an essential structural component of nearly all compounds embraced by the term lipid. More than half of the fatty acids encountered in Nature are unsaturated. Neither term—"fatty acid" or "unsaturated"—is unequivocally defined and each is used with various meanings in the literature.

While "fatty acid" formerly meant only a long-chain unbranched monocarboxylic acid, the name is nowadays frequently applied to all acids occurring in lipids. Modern analytical methods have shown that the latter definition covers an extremely heterogeneous group of compounds[1–3].

Used in the broadest sense, the term "unsaturated fatty acids" refers to all acids found in lipids whose carbon skeleton contains at least one multiple bond. These may be *cis* or *trans* double bonds or also triple bonds. Most natural unsaturated fatty acids only contain *cis* double bonds (Fig. 1). Nevertheless, it is common practice to apply the generic name "unsaturated fatty acids" to these compounds. The designations "polyenoic acids" and "polyunsaturated fatty acids (PUFA)" are used synonymously for all acids possessing two or more double bonds.

This review is concerned with unsaturated fatty acids in the narrower sense, *i.e.* only those acids having *cis* double bonds, encountered mainly in the animal kingdom, are considered.

While it was originally the science of nutrition which was primarily concerned with unsaturated fatty acids as "essential nutrients" and even assigned them a temporary place among the vitamins (vitamin F)[4], contemporary interest comes mainly from membrane research and prostaglandin research. It became apparent that, *e.g.*, the functions of membranes are closely related to the properties of the unsaturated fatty acids they contain, and that sensitive methods for assay of unsaturated fatty acids and the possibility of synthesizing radioactively labeled compounds of this kind are essential conditions for the study of many biological questions.

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2. Structure and Nomenclature

Unsaturated fatty acids occur in large numbers in practically all living creatures. The unsaturated fatty acids of animal lipids display a particular diversity in their molecular structure. The carbon chains have up to 28 carbon atoms[1]; and some acids have up to seven double bonds[5]. The structures of the acids (Fig. 1) display three common features:

1) The double bonds possess a *cis* configuration;

2) the double bonds are always separated by only *one* methylene group (divinylmethane or polyallyl rhythm); and

3) the first double bond is separated from the carboxyl group by at least *two* methylene groups.

These common structural features reveal common biosynthetic principles[6, 7] (Section 6.1).

$$CH_3-(CH_2)_x-\left[\underset{H}{C}=\underset{H}{C}-CH_2\right]_y-(CH_2)_z-COOH$$

Fig. 1. General structural formula of the most common unsaturated fatty acids occurring in Nature. $x = 1, 4, 5$, and 7; $y = 1$ to 6; $z = 2$ to 7.

Fatty acids containing *trans* double bonds[2, 8] or triple bonds[2, 9] are extremely rare in the animal kingdom. Unsaturated acids whose double bonds are separated by more than one methylene group[1, 3] or by none at all[10] are also hardly encountered in animal lipids. Like the above *cis* unsaturated acids, however, they do frequently occur in fungi and microorganisms.

Saturated and unsaturated fatty acids were initially assigned trivial names, but only few acids are still known by these names, such as oleic acid, linoleic acid, and arachidonic acid. The IUPAC nomenclature has been generally accepted (cf. Table 1). However, the systematic names are often rather long and so various abbreviated notations have been proposed, of which the three most common are illustrated in Table 1.

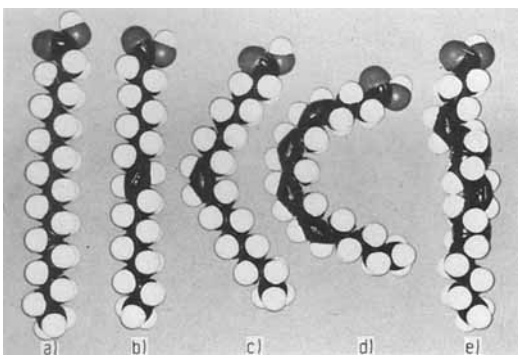
Table 1. Nomenclature of unsaturated fatty acids.

Trivial name	Systematic designation	Abbreviated notation		
		Klenk [7]	*Stoffel* [11]	*Holman* [12]
Oleic acid	*cis*-9-Octadecenoic acid	Δ^9-$C_{18:1}$	$18:1^9$	9-18:1
Elaidic acid	*trans*-9-Octadecenoic acid	*trans*-Δ^9-$C_{18:1}$	*trans*-$18:1^9$	*trans*-9-18:1
Linoleic acid	all-*cis*-9,12-Octadecadienoic acid	$\Delta^{9,12}$-$C_{18:2}$	$18:2^{9,12}$	9,12-18:2
α-Linolenic acid	all-*cis*-9,12,15-Octadecatrienoic acid	$\Delta^{9,12,15}$-$C_{18:3}$	$18:3^{9,12,15}$	9,12,15-18:3
γ-Linolenic acid	all-*cis*-6,9,12-Octadecatrienoic acid	$\Delta^{6,9,12}$-$C_{18:3}$	$18:3^{6,9,12}$	6,9,12-18:3
Arachidonic acid	all-*cis*-5,8,11,14-Eicosatetraenoic acid	$\Delta^{5,8,11,14}$-$C_{20:4}$	$20:4^{5,8,11,14}$	5,8,11,14-20:4

In addition, another nomenclature is frequently used in which the positions of the double bonds are given relative to the methyl end of the molecule[13]. α-Linolenic acid is then 18:3 (ω−3) and γ-linolenic acid 18:3 (ω−6), *i.e.* in the former case the third-from-last carbon atom belongs to the first double bond in the methyl end CH_3—CH_2—CH=CH, and in the second case the sixth-from-last CH_3—$(CH_2)_4$—CH=CH. This method of designation was chosen in order to express biogenetic relations of the acids in their names (Section 6.1.3).

3. Conformation and Physical Properties

Unsaturated fatty acids have physical properties differing from those of the corresponding saturated acids. This is because the double bonds modify the shape of the molecules. In the solid phase the hydrocarbon chain of saturated fatty acids preferentially adopts an extended conformation (Fig. 2a)[14]. In contrast, acids having a *cis* double bond exhibit a kink at the site of the *cis* double bond (Fig. 2c)[15]. With highly unsaturated acids having several *cis* double bonds this leads to a U-shaped or even ring-shaped form (Fig. 2d)[16]. A helical structure is also conceivable as a further strain-free conformation for all-*cis* unsaturated fatty acids (Fig. 2e)[17].



A 86.2

Fig. 2. Stuart-Briegleb models of a) stearic acid; b) elaidic acid; c) oleic acid; d) arachidonic acid—U form; e) arachidonic acid—helical form.

A *trans* double bond has a less drastic influence on the conformation. It effects a parallel shift of the aliphatic groups attached to the double bond in question. The molecule retains its extended shape (Fig. 2b). Hence the physical properties of acids containing *trans* double bonds resemble those of the saturated acids more closely than those of the *cis* compounds. This will now be illustrated with the aid of melting points.

This example was chosen because the temperatures of phase transitions play an increasingly important role in explanations of the properties of biological membranes (Section 7).

For example, oleic acid (*cis*-9-octadecenoic acid) melts at 10—11 °C[18], while the melting point of the *trans* isomer, elaidic acid (44.5—45.5 °C), is much closer to that of the corresponding saturated acid (stearic acid, 69.5 °C)[14]. That this is not an isolated case can be seen from Fig. 3a. The same rule applies to acids having two double bonds (Fig. 3b). Moreover, the two curves in Figure 3 clearly show that

the melting point of an unsaturated acid depends not only on the geometry of the double bonds but also on their position in the hydrocarbon chain. The melting point of an acid having *cis* double bonds deviates most from that of the corresponding saturated acid if the double bonds are located at or near the middle of the molecule. This position of the *cis* double bonds is also found most frequently in naturally occurring acids: *e.g.* oleic (9—18 : 1), vaccenic (11—18 : 1), linoleic (9,12—18 : 2), and plamitoleic acid (9—16 : 1) (concerning the abbreviations, see Table 1).

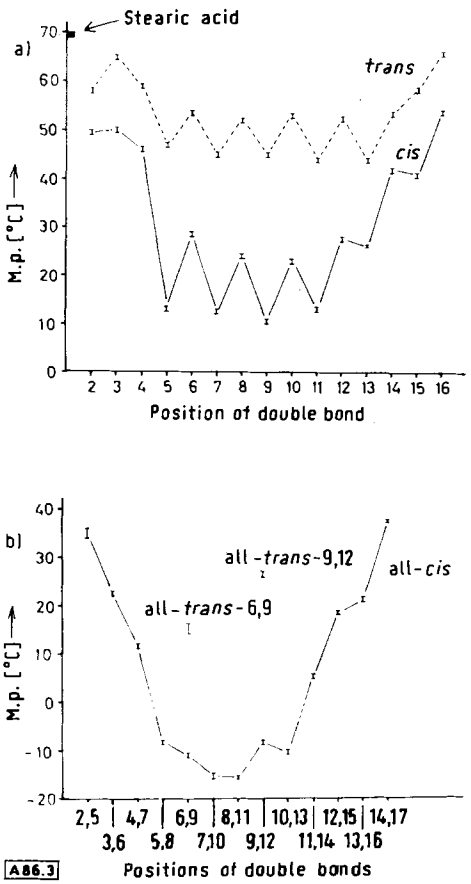


Fig. 3. Melting points of a) complete series of *cis*- and *trans*-octadecenoic acids [14, 18], and b) complete series of all-*cis*-octadecadienoic acids and of 6,9- and 9,12-all-*trans*-octadecadienoic acid [19, 20].

Table 2. Melting points of some all-*cis*-polyenoic acids.

Name	M.p. [°C]	Ref.
all-*cis*-9,12-Octadecadienoic acid	−8 to −9	[19]
all-*cis*-11,14-Octadecadienoic acid	4.5 to 5.5	[19]
all-*cis*-9,11-Octadecadienoic acid	19 to 20	[21]
all-*cis*-11,15-Octadecadienoic acid	11	[22]
all-*cis*-9,12,15-Octadecatrienoic acid	−10	[23]
all-*cis*-5,8,11,14-Eicosatetraenoic acid	−49.5	[23]
all-*cis*-5,8,11,14,17-Eicosapentaenoic acid	−54	[23]

The melting points of some isomeric all-*cis*-octadecadienoic acids listed in Table 2 demonstrate that the second characteristic structural feature of natural unsaturated fatty acids—the polyallylic rhythm—also leads to a lower melting point than is found for acids whose double bonds are either conjugated or isolated by more than one methylene group. Apart from geometry and position of the double bonds as well as the polyallylic rhythm, the number of double bonds also affects the melting point of an unsaturated acid.

The structural features of the natural unsaturated fatty acids—*cis* and not *trans* configuration, double bonds isolated by a methylene group and not conjugated—which appear remarkable from an energetic viewpoint, all combine in endowing the acids with a low melting point.

Numerous factors determine whether the fatty acid molecules adopt the above conformations or others. Importance attaches to the temperature and thus to the state of aggregation. In the crystalline phase a closely packed regular arrangement of molecules is favored[14, 24]. The molecular organization in the liquid phase is largely determined by the environment. If the fatty acids are incorporated into lipids then the intramolecular environment already influences the conformation of the hydrocarbon groups. In polar solvents at concentrations exceeding a characteristic value for each species, *i.e.* the critical micellar concentration, polar lipids (salts of fatty acids, phospholipids, sphingolipids, and free fatty acids) form micelles. In apolar solvents the solvent molecules intervene between the hydrocarbon chains and suppress their interaction[25], partly or completely. This becomes increasingly difficult the greater the London-van der Waals forces are between the chains, *i.e.* the denser the packing of the fatty acid groups. It therefore follows that the solubility of fatty acids in apolar solvents increases with decreasing chain length and increasing number of double bonds[26].

Apart from the crystalline phase and liquid phases, some lipids and lipid mixtures can also form liquid crystalline phases in which the hydrocarbon groups are "molten" (mesophases)[27]. In this state, the individual fatty acids have a greater degree of thermal freedom than in the crystalline phases; however, the overall orientation of the lipid molecules is retained within a wide range of extension in one, two, or three dimensions[28]. The degree of fluidity of the hydrocarbon chains has not yet been elucidated[29]. The crystalline/liquid crystalline phase transition temperatures for lipids depend, *inter alia*, upon the nature of the fatty acids, as do the capillary melting points[30, 31]. For lipids which differ only in their fatty acid composition, those containing acids with *cis* double bonds have lower transition temperatures than the lipids containing saturated acids[32]. These temperatures lie far below the capillary melting points. For instance, transition of dipalmitoyl phosphatidylcholine occurs at 40 °C, whereas the capillary melting point is 230 °C. In the case of dioleoyl phosphatidylcholine the phase transition takes place at −22 °C[30].

All interpretations of differing physical properties of saturated fatty acids, *cis* and *trans* unsaturated fatty acids, as well as lipids containing these acids, are based on the concept that the various conformations of the acids have different spatial requirements (see Fig. 2). Studies on monomolecular lipid films at the water-air interface confirmed these ideas[33]. Such investigations showed that the area required per molecule is higher for lipids with *cis*-unsaturated acids than for corresponding lipids with *trans*-unsaturated or saturated acids.

Reversible transitions of molecular organization in lipids are at the center of intense study because there are indications that these transitions also take place in biological membranes and are of fundamental significance for their functioning (Section 7).

4. Chemical Synthesis[34, 35]

The simplest unsaturated fatty acid, oleic acid, was first prepared in 1934[36]. It was not until 1950 that the first acid with two double bonds, linoleic acid, was simultaneously synthesized by three independent research teams[37, 38]. The principal difficulty of this synthesis is met in avoiding formation of *trans* configurated double bonds or positional isomers alongside the desired *cis* double bonds—a problem that becomes increasingly difficult to solve as the number of double bonds increases. The crucial breakthrough only came with development of the "acetylenic approach"[34, 35, 39]. This consists of an initial synthesis of acids containing triple bonds instead of *cis* double bonds at the correct positions of the molecule; in the final synthetic step these are reduced selectively and stereospecifically to *cis* double bonds. Since all double bonds are introduced simultaneously the likelihood of undesired isomerizations of the *cis* double bonds is limited to the final reaction step of the synthetic sequence.

Attempts have also been made to prepare unsaturated fatty acids by Wittig reaction[40, 41]. Although the stereochemical course of this reaction is largely controllable[40], the approach is unsuitable for construction of highly unsaturated fatty acids containing up to seven double bonds owing to the reaction conditions[35]. The *cis* double bonds can only be introduced successively by this method and the probability of isomerization is therefore high. So far only oleic and linoleic acids have been synthesized with the aid of the Wittig reaction[40, 41]. However, the method has provided valuable results in the preparation of some unsaturated fatty acids having *trans* double bonds or triple bonds that are not readily accessible by the acetylenic approach[41, 42].

Synthesis of unsaturated fatty acids by the acetylenic approach raises two problems:

1) preparation of polyacetylenic acids whose triple bonds are each separated by *one* methylene group, and

2) transformation of the triple bonds into *cis* double bonds.

4.1. Preparation of Polyacetylenic Acids

Polyacetylenic compounds whose triple bonds are all separated by one methylene group are obtained exclusively by condensation of Grignard complexes of ω-alkynes with substituted propargyl halides or propargyl methanesulfonates (Fig. 4)[35, 39, 43, 44]. This reaction requires copper(I) chloride or cyanide as catalyst. Tetrahydrofuran is usually employed as solvent. Synthesis starts from a fitting "methyl end" and the desired carbon skeleton is built up stepwise, the "carboxyl end" being added in the last step (Fig. 5).

$$R^1\text{–}C{\equiv}C\text{–}CH_2\text{–}X + BrMg\text{–}C{\equiv}C\text{–}R^2 \longrightarrow R^1\text{–}C{\equiv}C\text{–}CH_2\text{–}C{\equiv}C\text{–}R^2 + MgBrX$$

Fig. 4. Condensation of the Grignard complex of an ω-alkyne with a substituted propargyl halide or methanesulfonate (X = Br, I, OSO_2CH_3) with Cu^I catalysis.

Initially, building blocks were used which contained one triple bond only, *i.e.* each triple bond was added individually (Fig. 5a). However, in recent years methods have been developed for synthesizing suitable units possessing two triple bonds[46, 47], thus considerably reducing the number of reaction steps (Figs. 5b, 5c)[47, 48].

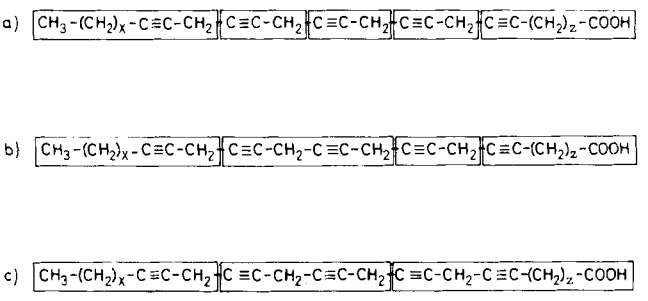


Fig. 5. Schematic survey of building blocks employed in synthesis of polyynoic acids illustrated for a pentaynoic acid. a) Strategy of *Osbond et al.* [39]. b) strategy of *van der Steen et al.* [45], c) strategy of *Kunau* [46].

The above Grignard reaction cannot be employed for preparation of suitable "methyl ends" since the Grignard derivatives of ω-alkynes react only with activated alkyl halides but not with saturated alkyl halides[43]. These starting compounds are therefore prepared by coupling of metal acetylides with alkyl halides in liquid ammonia[43, 44].

So far the most frequently used substituted propargyl halides have been the bromides[34, 39, 45, 47, 49] since the corresponding chlorides are not reactive enough and the iodides were inaccessible until recently[50]. Meanwhile the iodides have proved to be superior to substituted propargyl bromides, especially during the final condensation[48]. The use of substituted propargyl methanesulfonates has hitherto been precluded by their poor accessibility[37] and no systematic study of their application in this reaction has yet been undertaken. However, recent experiments have shown that substituted propargyl methanesulfonates can be prepared in high yield by the method of *Crossland et al.*[51] and that they also react with the Grignard complexes of ω-alkynes[52].

The polyacetylenes and polyacetylenic acids thus obtained are labile substances[53]. Their sensitivity to light and heat becomes all the greater the more triple bonds are present in the molecule and is further enhanced by the presence of terminal 1,4-pentadiyne or even 1,4,7-octatriyne structures[54]. This greatly hinders purification by distillation. Polyynoic acids often polymerize at temperatures between 50 and 100 °C[39, 47]. Above 150 °C spontaneous polymerization may occur.

These acids can be stored only in pure crystalline form at −30 °C for weeks or months. pH values exceeding 7 should be avoided since 1,4-pentadiyne structures readily rearrange to 1,3-diyne and allene structures[55].

4.2. Transformation of Triple Bonds into *cis* Double Bonds

The acetylenic approach requires not only preparation of suitable polyacetylenic acids but also conversion of triple bonds into *cis* double bonds. Use of this method became feasible only on discovery of a catalyst possessing the necessary selectivity—reduction of triple bonds but not of double bonds—and stereospecificity—formation of *cis* but not of *trans* double bonds[56]. The catalyst concerned is composed of palladium on calcium carbonate and contains lead(II) ace-

tate—it is known as the Lindlar catalyst. The required selectivity is achieved by admixture of quinoline.

By-products of partial hydrogenation include acids containing fewer double bonds than there were triple bonds in the polyacetylenic acid to be hydrogenated. Furthermore, acids having one or several *trans* double bonds are also found. The amount of by-products formed depends upon the number of triple bonds in the polyacetylenic acid undergoing partial hydrogenation. Their formation is explained by isomerization and/or hydrogenation of intermediates possessing double bonds in β-position relative to the triple bonds[57]. The desired all-*cis*-polyenoic acid is purified by chromatography on silica gel impregnated with silver nitrate (Section 5.2)[58].

In some cases hydroboration has been used for partial reduction of triple bonds. It was found that boranes with two large bulky groups, *e.g.* diisoamylborane (disiamylborane) can partially reduce triple bonds. This was accomplished not only with a few selected small molecules containing *one* triple bond[59] but also with a series of *poly*ynoic acids[60]. Detailed studies on the selectivity and stereospecificity that can be achieved have yet to be performed.

4.3. Synthesis of Radioactively Labeled Unsaturated Fatty Acids

Replacement of hydrogen by tritium atoms in existing polyenoic acids by the Wilzbach method is unsuitable for preparing radioactively labeled unsaturated fatty acids since hydrogenation of the double bonds takes place[61]. The radioactive label must therefore be introduced during synthesis of the molecule. Two different methods have been adopted for this purpose. The first technique started from unsaturated acids isolated from biological sources and ^{14}C was introduced by chain extension by one (nitrile synthesis) or two carbon atoms (malonic ester synthesis), either directly or after prior partial degradation[62]. Once the total synthesis of unsaturated fatty acids had become possible a second pathway opened up. The reactions of the acetylenic approach were varied in such a manner that the resulting unsaturated acids were labeled either with ^{3}H or with ^{14}C in certain positions[35].

Labeling of the double bonds with tritium is accomplished by partial hydrogenation of polyynoic acids in the presence of tritium. It has not yet been possible to label just one specific position with tritium by the acetylenic approach, although that aim has been achieved by chemical synthesis employing exclusively the Wittig reaction for the preparation of oleic acid and linoleic acid[63]. Higher unsaturated fatty acids stereospecifically tritium-labeled at only one C atom (D or L form) have been obtained by biochemical reactions[64, 65]. The double bonds were introduced into the stereospecifically labeled saturated acid with the aid of microorganisms.

Double labeling with ^{14}C and ^{3}H has so far only been carried out on rare occasions[11, 66, 67]. For most biological applications mixtures of acid molecules labeled with either ^{3}H or ^{14}C prove to be adequate[65].

5. Analysis

Owing to close structural similarities between unsaturated fatty acids, analysis of these substances cannot be based on pronounced differences in their chemical reactivity but is compelled to exploit slight differences in physical properties. This follows directly from the molecular structure of the unsaturated acids which deviate from one another in three parameters only, *i.e.* chain length, and number and positions of the double bonds. Only the double bonds are open to chemical attack. The analytical methods used nowadays for separation and identification of unsaturated acids are admittedly of an advanced technical standard but no method is yet available which permits simultaneous determination of all three parameters even though gas chromatography has been very close to doing so in some cases.

As with other natural products, the problem rarely arises of having to determine the structure of a single pure acid, as for example on completion of a synthesis; usually the unknown acid is present in a mixture and must first be isolated from other acids. Matters are often further complicated by the availability of only milligram or microgram quantities of sample.

5.1. Chemical Methods

Most chemical methods for the analysis of unsaturated fatty acids[58] have meanwhile been displaced by physical techniques and nowadays possess only historical interest. The sole method that is still in common use and has remained unsurpassed in its information yield is the degradation of unsaturated fatty acids by ozone (Fig. 6)[68]. The ozonides formed on ozonolysis can be reduced by triphenylphosphane, dimethyl sulfide, or hydrogen, oxidized by hydrogen peroxide, glacial acetic acid, or performic acid, or pyrolyzed, each mode of treatment giving characteristic fragments depending upon the position of the original double bonds. The fragments can be identified by gas chromatography. Since the fragments arising from methylene groups between the double bonds—*i.e.* malondialdehyde or malonic acid—cannot be quantitatively determined, ozonolysis performed in this way only yields information about the positions of the first and last double bonds but not about the chain length or the number of double bonds. The number and positions of the double bonds can be established by partial ozonolysis[69] or by partial hydrogenation with hydrazine prior to the ozonolysis[70]. The chain length has to be determined by other methods such as gas chromatography of a completely hydrogenated sample (Fig. 6).

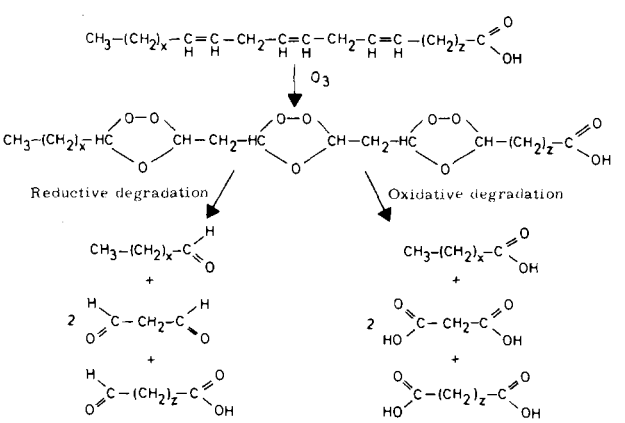


Fig. 6. Ozonolysis of a trienoic acid with subsequent reductive or oxidative ozonide cleavage.

Proof of a structure by ozonolysis must be preceded by isolation of the compound concerned, since the fragments obtained by ozonolysis cannot be assigned to the individual acids. The amount of sample required for this method depends both upon the sensitivity of the detector used for the gas chromatography and also upon the extent to which side reactions can be suppressed during ozonolysis and losses reduced during workup of the cleavage products. A 0.5-mg sample of a pure unsaturated acid usually suffices for structural elucidation by ozone degradation.

5.2. Chromatographic Methods

Analysis of small amounts of unsaturated fatty acids got under way only after development of chromatographic techniques and once authentic samples had become available for comparison. Whereas column chromatography is employed for separation of large amounts of fatty acid mixtures[71], the isolation and identification of small amounts of unsaturated fatty acids is accomplished with gas chromatography[58, 72].

The stationary phases available today permit extensive resolution of the fatty acid mixtures found in nature into their individual components after prior conversion into the methyl esters (Fig. 7). However, structural assignment can only be accomplished by comparison of retention times with those of authentic samples. The similar retention times observed for the methyl esters of many fatty acids (Fig. 7a) sometimes necessitates confirmation of the structure by an independent method.

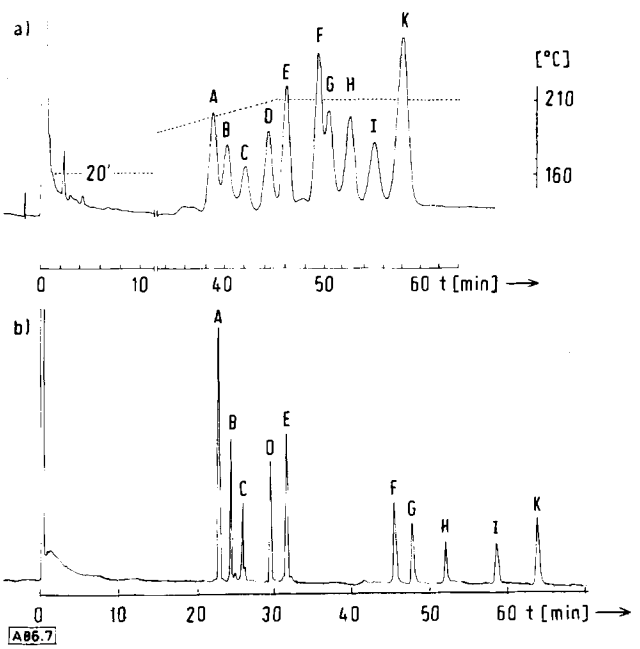


Fig. 7. Gas chromatograms of a synthetic mixture of methyl polyenoates [74] (for abbreviations see Table 1). a) Packed column, 6% DEGS (diethylene glycol succinate), 1.80 m long, glass, 4 mm i.d., temperature program. b) Capillary column, FFAP (free fatty acid phase), 87 m, glass, 0.25 mm i.d., 180 °C. A: 5,8,11—20:3; B: 8,11,14—20:3; C: 5,8,11,14—20:4; D: 8,11,14,17—20:4; E: 5,8,11,14,17—20:5; F: 4,7,10,13—22:4; G: 7,10,13,16—22:4; H: 4,7,10,13,16—22:5; I: 7,10,13,16,19—22:5; K: 4,7,10,13,16,19—22:6.

Capillary column gas chromatography is a considerable improvement: differences in retention times and hence the separating power are greater (Fig. 7b)[73, 74]. However, the columns can only be loaded with a tenth to a hundredth of the amount of material that can be applied to a packed column and the method is therefore unsuitable for preparative purposes.

Thin layer chromatography on silica gel impregnated with silver nitrate is used to separate fatty acid mixtures into fractions which each contain acids having the same number of double bonds[75]. As the number of double bonds increases, the mobility of these coordination complexes in the liquid phase decreases. *Cis* and *trans* isomers can also be separated in this way[76].

5.3. Spectroscopic Methods

While chromatographic methods are indispensable in the separation of polyenoic acids, they are surpassed by spectroscopic techniques in structural analysis. Although UV and IR spectroscopy admittedly revealed only the number[58] or configuration[77] of double bonds, the position of the double bonds has also been established alongside their configuration[78] for a number of polyenoic acids by proton resonance spectroscopy[79, 80]. Systematic studies with complete series of octadecenoic and octadecadienoic acids have shown that unequivocal differentiation of positional isomers by proton resonance spectra is feasible only when the double bonds are not located in the center of the molecule[81]. However, this difficulty can be overcome by the use of shift reagents[80].

Another promising method for the analysis of fatty acids is mass spectrometry. Although polyenoic acids themselves do not give fragmentation patterns betraying the number and positions of the double bonds owing to the ready electron-impact induced migration of the double bonds, such patterns are obtained with their derivatives. Reactions are carried out at the double bonds to give compounds which undergo preferential cleavage between the carbon atoms of the original double bonds and thus lead to characteristic fragments of sufficient intensity.

Studies of this kind have been performed mainly with compounds having one double bond. However, the derivatives used for monoenoic acids are unsuitable for polyenoic acids since the fragmentation schemes are then too complicated[82]. So far only methyl[82, 83] and trimethylsilyl ethers[82] have been used in structural elucidation of polyenoic acids possessing up to five double bonds. The primary fragments of both derivatives tend to lose their ether groups; this occurs in a predictable manner in the trimethylsilyl derivatives[82]. Of the originally vicinal trimethylsilyl groups, only one is left in the resulting fragments. In contrast, the primary fragments of the methyl ether derivatives lose all methoxy groups with equal probability, giving a variety of product fragments in roughly equal abundancies[82, 83]. Therefore the characteristic fragments for localization of the double bonds have much higher intensities in the mass spectra of the trimethylsilyl derivatives than in those of the methyl ether derivatives.

A method of obtaining informative fragmentation patterns without chemical modification of the double bonds has recently been the subject of discussion[84]. Use of substituted amides in place of the saturated acids or their esters should lessen the extent of electron-impact induced migration of the double bonds owing to localization of the positive charge

on the nitrogen. This has meanwhile been successfully implemented for monoenoic acids[85].

Although structural elucidation of unsaturated fatty acids by mass spectrometry requires a pure sample, only microgram quantities are required; combination of gas chromatography and mass spectrometry is therefore an obvious choice for analysis of mixtures. However, initial expectations have not yet been fulfilled: it has so far proved impossible to derivatize a mixture of polyenoic acids in such a way that all the components are present in the same proportions as before derivatization; moreover, the derivatives cannot yet be separated as well as the polyenoic acids themselves in the chromatographic step[82].

6. Metabolism

6.1. Biosynthesis

Starting from acetyl-CoA, saturated fatty acids are built up by the same metabolic pathways in microorganisms, plants, and animals. The enzymes required for this *de novo* synthesis are present as a multienzyme complex—fatty acid synthetase—in yeasts[86], in the alga *Euglena gracilis*[87] under heterotrophic growth conditions, and in the animal kingdom[88, 89]; in contrast, the individual enzymes were isolated from bacteria[90] and plants[91]. The major final product of the *de novo* synthesis in animal cells is palmitic acid ($C_{15}H_{31}COOH$), together with small amounts of myristic ($C_{13}H_{27}COOH$) and stearic acid ($C_{17}H_{35}COOH$)[89].

These *saturated* acids serve as precursors for biosynthesis of the *unsaturated* acids. Since the double bonds are introduced independently of chain elongation this metabolic pathway requires two further enzyme systems:

1) *desaturases*, which introduce *cis* double bonds in an oxygen-dependent reaction, and

2) *enzymes of chain elongation*, which lengthen the final products of the *de novo* synthesis and the desaturase reaction by further C_2 units.

6.1.1. Aerobic Formation of Double Bonds

Except for obligate and facultative anaerobes, introduction of double bonds into the hydrocarbon chain of fatty acids in Nature always occurs independently of the reactions involved in the *de novo* synthesis. In anaerobes the double bonds are already introduced *anaerobically* by fatty acid synthetase during formation of the carbon skeleton by elimination of water from hydroxylated intermediates[92]. Further chain elongation or the presence of desaturases has not been observed in these organisms.

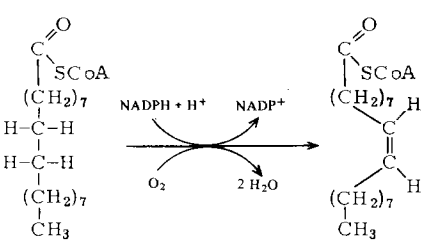


Fig. 8. Aerobic formation of a double bond.

The precise mechanism of formation of isolated *cis* double bonds within a completed carbon chain by desaturases has not yet been entirely elucidated. As far as is known, it is basically the same for microorganisms[92], plants, and animals[93–96] (Fig. 8). The reaction is strictly *aerobic*, the oxygen cannot be replaced by other electron acceptors; reduction equivalents are supplied by NADH or NADPH. These facts favor a mechanism resembling that operative in reactions catalyzed by mixed function oxygenases[97]. However, no hydroxylated products could be detected as intermediates[98, 99].

Removal of hydrogen atoms during formation of the *cis* double bond is strictly stereospecific. This was first established for the conversion of tritiated stearic acid into oleic acid in *Corynebacterium diphtheriae*[100]. D hydrogen atoms are detached stereospecifically from the two prochiral centers, at C-9 and C-10, on formation of the double bond (Fig. 9). The same was found in work with the alga *Chlorella vulgaris* and with chicken liver[99, 101, 102]. These experiments were performed to study the synthesis of oleic acid from stearic acid and of linoleic acid from oleic acid. The stereochemical course was the same as in the bacterial system for introduction of both the first and the second double bond. The hydrogen atoms removed were *erythro* configurated relative to each other, and furthermore, of the four possible hydrogen atoms, only the two having the D configuration were eliminated. The observed kinetic isotope effects[102, 103] suggest that the two hydrogen atoms are removed simultaneously. This would explain the failure of all previous searches for an oxygenated intermediate.

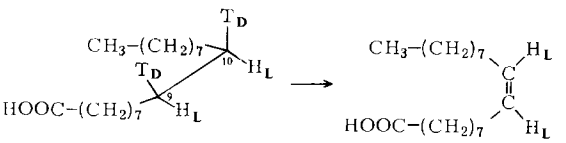


Fig. 9. Stereochemistry of hydrogen elimination in the desaturase reaction.

Although the carboxyl group of the acids does not participate directly in formation of the double bonds, acids are accepted as substrates for desaturases only if the carboxyl group is not present in free form. In animal cells[95] and bacteria[100, 104] only the coenzyme A esters are suitable substrates while in plants desaturases have been found which require the acyl carrier protein (=ACP) derivatives of the acids[93, 105]. Again in contrast to animal cells, it has been proved in some cases for microorganisms that double bonds can also be formed in fatty acid molecules incorporated as acyl groups into complex lipids[106].

Participation of an electron transport chain, *i.e.* a series of proteins transferring electrons from the electron donor NADH or NADPH to the electron acceptor O_2, has been verified for some desaturases. The most detailed knowledge available pertains to a desaturase complex of the alga *Euglena gracilis*[105] since the proteins involved are not bound to membranes, as they are in all other cases investigated so far.

As in *Euglena gracilis*, three proteins are involved in the reaction in rat liver (Fig. 10): a flavoprotein which oxidizes the reduced pyridine nucleotides, transferring the electrons to the second protein (ferredoxin in *Euglena gracilis* or cytochrome b_5 in rat liver). The third protein is most probably the actual O_2-activating enzyme possessing desaturase activity. In rat liver it is inhibited by cyanide and for this reason it is designated cyanide-sensitive factor (=CSF)[107].

These two desaturase complexes, which have been most thoroughly studied up to now, catalyze the transformation of activated stearic acid into activated oleic acid. However, the formation of oleic acid is merely the first step in the biosynthesis of polyunsaturated acids from stearic acid; apart from chain elongation, additional double bonds are introduced in polyallylic rhythm. There is evidence that various desaturases possessing pronounced specificity towards the substrate and the product are involved[96].

A strong indication of the existence of desaturases having different substrate specificity is provided by the fatty acid spectrum of various organisms. Bacteria contain only monounsaturated acids[108]. They synthesize mainly palmitoleic and/or oleic acid from palmitic and stearic acid but cannot introduce any more double bonds into these monoenoic acids. Plant cells are able to do so; they transform stearic acid into oleic, linoleic, and α-linolenic acid[109]. Animal cells are incapable of introducing a second or third double bond into the methyl end of oleic acid[110], but do synthesize more highly unsaturated acids from linoleic and α-linolenic acid if they are administered together with nutrients[111, 112].

The marked action specificity of desaturases is illustrated by the formation of α- or γ-linolenic acid from linoleic acid (Fig. 11). In plants linoleic acid is transformed into α-linolenic acid by introduction of the third double bond in position 15, 16, a reaction beyond the capability of the animal cell. However, in contrast to plants, the latter can introduce the third double bond in position 6, 7 of linoleic acid and thus synthesize γ-linolenic acids.

Evidence so far available on the substrate and action specificity of desaturases suggests that the biosynthesis of 4,7,10,13,16,19-docosahexaenoic acid will require as many as six different desaturases.

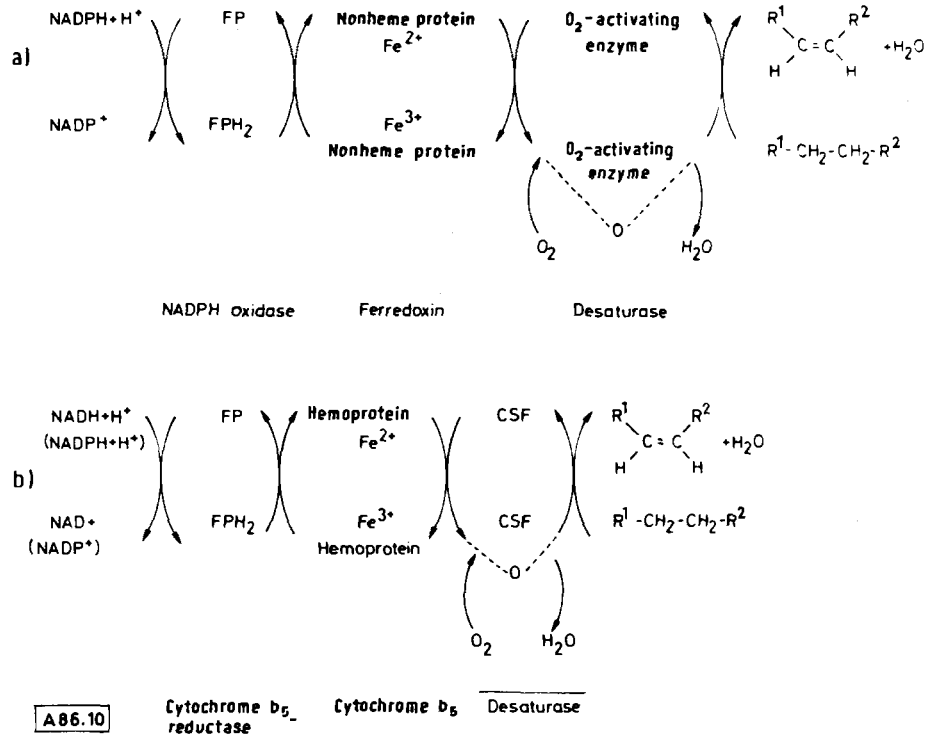


Fig. 10. Electron transport chain for oxygen activation in the desaturase reaction a) in *Euglena gracilis* (according to ref. [92]), b) in the animal organism. FP = flavoprotein, CSF = cyanide sensitive factor.

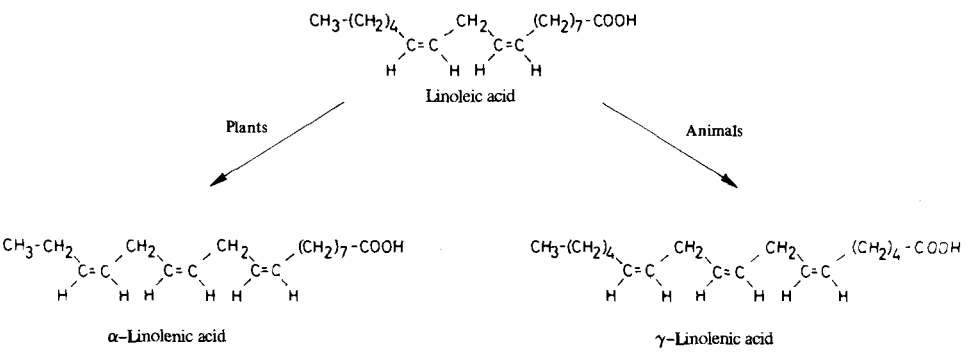


Fig. 11. Specificity of desaturases towards the product. Formation of α- and γ-linolenic acid from linoleic acid.

6.1.2. Chain Elongation

Chain elongation of fatty acids formed in the *de novo* synthesis by fatty acid synthetase is a metabolic process encoun-

tered in numerous eukaryotic microorganisms[113, 114] and in the animal kingdom[111, 112, 115–117]. It is still open whether bacteria and plants also possess enzymes for a chain elongation distinct from the *de novo* synthesis. A malonyl CoA dependent chain elongation has occasionally been observed in plant waxes and bacterial species having exceptionally long fatty acids[118]. Moreover, there is evidence that chain elongation participates alongside *de novo* synthesis in the biosynthesis of C_{18} acids in plants[119].

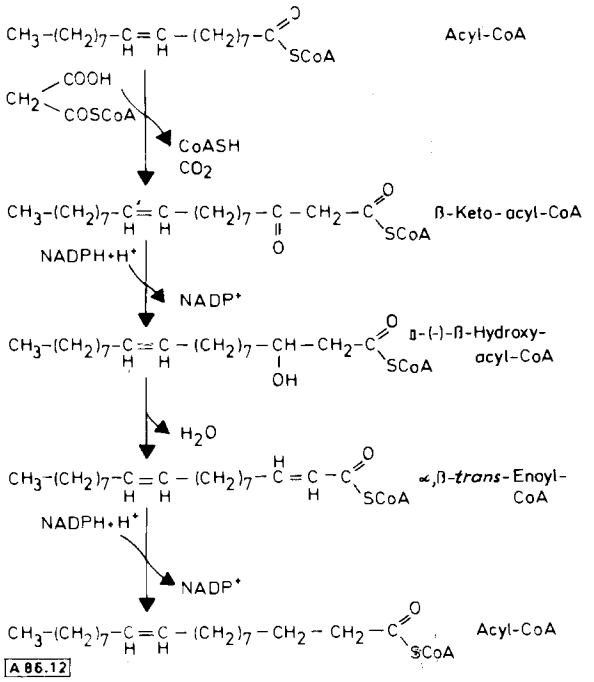


Fig. 12. Course of chain elongation by two carbons, illustrated for oleic acid.

In animal cells the enzymes responsible for chain elongation are located, like the desaturases, on the membranes of the endoplasmic reticulum[115–117]. They have so far resisted all attempts at isolation. All the properties known today have been deduced from experiments on membrane fragments of the endoplasmic reticulum (microsome fraction). The mechanism of chain elongation was established in this way[115, 116] (Fig. 12): the substrates are the coenzyme-A esters of saturated and unsaturated fatty acids which condense with malonyl CoA in the first step, the carboxyl group of the malonyl CoA being liberated as CO_2. As product, this reaction yields a β-keto thioester that is converted, *via* a D-(−)-β-hydroxy- and an α,β-*trans*-enoyl thioester in the three subsequent steps, into the acyl CoA compound, which differs from the starting material by having two additional methylene groups. Hence the same reactions occur as in the *de novo* synthesis on fatty acid synthetase. In both cases the carbon skeleton is extended by two carbon atoms in a cycle of four reactions. This is the reason why both the saturated and the unsaturated fatty acids occurring in Nature exhibit an even number of carbon atoms. However, a fundamental difference between this chain elongation and the *de novo* synthesis is that all the intermediates are present as CoA esters and are not enzyme bound as in the latter case[115, 116].

Most of the studies on chain elongation were performed with microsomal fractions from rat liver. It was found that the optimum substrate specificity of the participating enzymes lies at 10—16 carbon atoms for saturated acids[115]. However, if fatty acids containing more than 16 carbon atoms have two or more *cis* double bonds then they are consumed just as fast as the shorter saturated acids, if not faster[115, 116]. The positions of the double bonds exert an additional effect. The shorter the carboxyl end, *i.e.* the smaller the value of *z* (Fig. 1), the better the unsaturated acids are elongated[116].

It is still largely uncertain whether each one of the four reactions of chain elongation involves just one enzyme of low chain length specificity or several of high specificity. Only in the case of mouse brain endoplasmic reticulum has the existence of three independent elongation systems, strictly specific for chain lengths of 16, 18, and 20 carbon atoms respectively, been established[120].

Apart from the microsomal chain elongation described so far, an ubiquitous mitochondrial enzyme system is also known[121, 122]. It utilizes acetyl CoA instead of malonyl CoA as C_2 donor[123], but the reaction sequence is otherwise identical. The first three steps of acetyl CoA dependent chain elongation appear to be the reversal of the β-oxidation reactions. The fourth reaction, reduction of the α,β-*trans* unsaturated CoA ester, is again catalyzed by a 2-enoyl-CoA reductase, as in chain elongation on the endoplasmic reticulum[122, 124]. This makes the reversal of β-oxidation thermodynamically feasible[122].

The function of mitochondrial chain elongation and its quantitative contribution to the synthesis of fatty acids is a matter of dispute. Reasons of cellular economics would appear to counterindicate an all too important role in the biosynthesis of unsaturated fatty acids. Since the desaturase reaction is restricted solely to the microsomal fraction, the substrates and products of this reaction would have to be transported into the mitochondria prior to chain elongation and removed again afterwards. However, the inner mitochondrial membrane is impermeable to CoA esters[125], which would therefore have to be converted into carnitine esters prior to each transport step[126]. These transport processes are not necessary for chain elongation by the microsomal enzymes. Recent investigations suggest that the function of mitochondrial chain elongation is to be sought in energy metabolism[122]. A quantitative comparison of pork liver cell fractions has revealed that the activity of the microsomal chain elongation is five times greater than that in mitochondria[122a].

6.1.3. Fatty Acid Families and Patterns

The joint action of enzyme systems for chain elongation and introduction of *cis* double bonds on a single acid can lead to a variety of unsaturated fatty acids. They differ in chain length and in the number and positions of the double bonds. Since the desaturases present in animal tissues can only catalyze formation of double bonds in the "carboxyl end", and since chain elongation occurs at the carboxyl group, the unsaturated acids of animal organisms, which are formed by chain elongation and desaturation from the same starting acid, will all possess the same "methyl end". Biosynthetic relationships are reflected by the structures. All acids having the same methyl end are collected together as a "fatty acid family" (fatty acid type) named after the starting acid[111]. The principal starting substrates for the biosynthesis of highly unsaturated fatty acids in animal organisms are palmitoleic, oleic, linoleic; and α-linolenic acids.

The number of possible biosynthetic pathways leading to a particular polyenoic acid becomes greater and greater with the length of the acid and the number of double bonds it contains. The actual route adopted for formation of an unsaturated fatty acid depends upon the sequence of desaturase and elongation steps which can differ in different organisms (see Fig. 13).

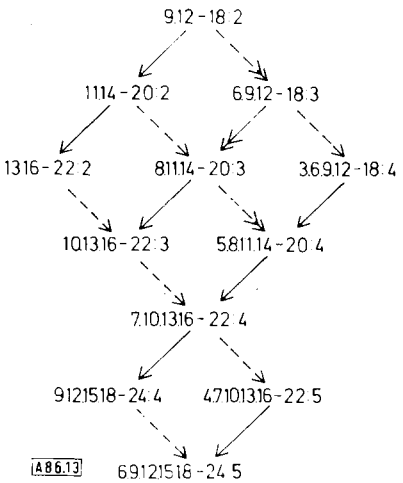


Fig. 13. Conceivable biosynthetic pathways of fatty acids belonging to the linoleic acid family. Participating reactions: chain elongation (→) and desaturase reaction (⇢). The double arrows indicate the preferred formation pathway of arachidonic acid (5,8,11,14-eicosatetraenoic acid) from linoleic acid in the rat (for abbreviations see Table 1).

Studies performed with the microsomal fraction of rat liver have suggested that the qualitative and quantitative composition of the fatty acids of a cell—*i.e.* the fatty acid pattern—may be affected not only by the different reaction rates of various acids in competing reactions[116] but also by the differing competitive inhibition exerted by the members of one fatty acid family on the reactions of acids belonging to another family[127].

Differences in the ability of microorganisms to synthesize unsaturated fatty acids have sometimes been employed to establish phylogenetic relationships[114]. If we restrict our attention to introduction of a third double bond into linoleic acid, there result three groups (Fig. 14). Group A comprises those organisms which form α-linolenic acid from linoleic acid and are thus capable of the reaction typical of the fatty acid metabolism of plants. Organisms of group C, like animal cells, can only convert linoleic acid into γ-linolenic acid. Group B contains all those microorganisms which can synthesize both α- and γ-linolenic acid. If this comparison is extended to include the differing ability to synthesize more highly unsaturated fatty acids, *i.e.* to form further double bonds and elongate the carbon chain, a scheme can be drawn up which shows good agreement with that of phylogenetic development according to *Klein* and *Cronquist*[128].

6.2. Oxidation

Both unsaturated and saturated fatty acids are degraded by β-oxidation in mitochondria[116]. This is a sequence of four steps during which the first two carbon atoms are cleaved from the carboxyl end of an activated fatty acid as acetyl CoA[129]. This process is repeated until the last two carbon atoms of the methyl end of the fatty acid remain behind as acetyl CoA. According to their mechanism the steps involved in β-oxidation in mitochondria appear to be the reversal of the four reactions of *de novo* synthesis in cytoplasm and chain elongation in microsomes. However, malonyl CoA is used for construction while the two carbon atoms cleaved off are liberated as acetyl CoA.

Owing to the *cis* double bonds of unsaturated fatty acids, intermediates occur during their β-oxidation which do not appear on degradation of saturated acids[116, 130]. Hitherto it was assumed that they are 2-*cis*- and 3-*cis*-enoyl-CoA compounds. These thioesters can be transformed into "normal" β-oxidation intermediates by further reactions[131].

Thus 3-*cis*-enoyl compounds are isomerized to 2-*trans*-enoyl-CoA compounds (Fig. 15a). 2-*cis*-Enoyl CoA esters initially add water and form D-(−)-hydroxyacyl-CoA compounds which are subsequently converted into the L-(+) form and thus re-enter the β-oxidation cycle (Fig. 15b).

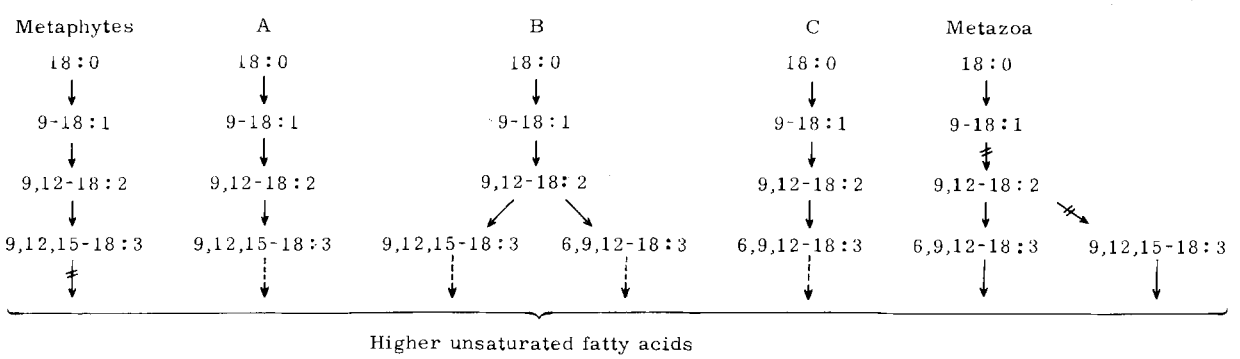


Fig. 14. Comparison of biosynthetic pathways for unsaturated fatty acids in various microorganisms with the synthetic pathways in plants and higher animals. Group A: microorganisms which, like plants, form α-linolenic acid (*e. g. Pyrrophyta, Ascomycetes, Basidomycetes*, yeasts, and *Chlorococcales*). Group B: microorganisms which synthesize both α- and γ-linolenic acids (*e. g. Rhodophyta, Euglenaphyta, Phaephyta, Vovocales, Chytridomycetes, Oomycetes*, and numerous species of *Cyanophytae*). Group C: microorganisms which, like animal cells, convert linoleic acid into γ-linoleic acid (*e. g. Zygomycetes, Sarcodina, Zoomastigophora*, and *Ciliophora*). ⇢: reactions which fail to occur owing to absence of enzymes. →: reactions occurring in some but not all microorganisms of this group.

Recent studies on the substrate specificity of acyl CoA dehydrogenases from bovine liver suggest that unsaturated fatty acids are not oxidized as far as the 2-*cis*-enoyl CoA esters but only up to the stage of 4-*cis*-enoyl CoA esters by β-oxidation[132]. Further degradation can only occur once

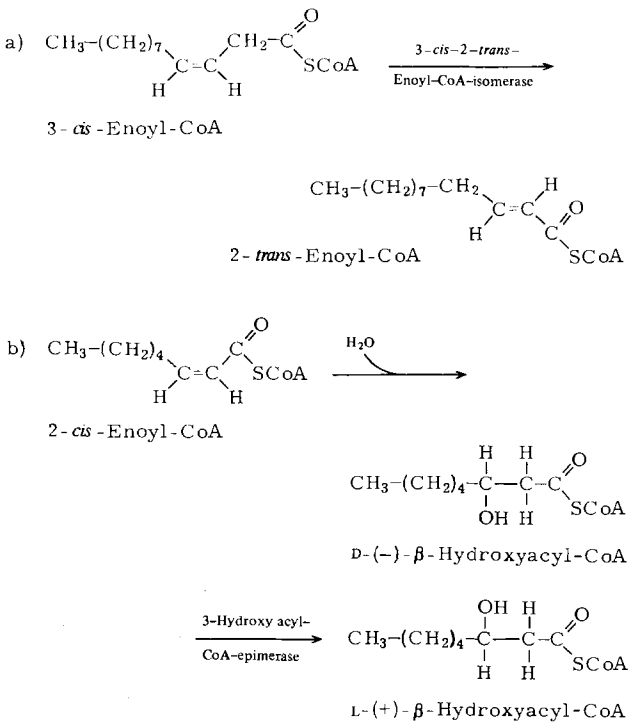


Fig. 15. Reactions which reintroduce the specific degradation intermediates of 2-*cis*-enoyl CoA ester (a) and 3-*cis*-enoyl CoA ester (b) into the β-oxidation cycle of saturated fatty acids.

the double bond in position 4 has been reduced. An enzyme, 4-enoyl CoA reductase, which catalyzes this reaction has been found in animal liver[67, 133].

In contrast to β-oxidation of saturated fatty acids[134], a partial degradation is found to occur with many polyunsaturated fatty acids; *i. e.* detectable amounts of intermediates accumulate[11, 135, 136]. These differ from the starting acids by loss of the first double bond and/or by chain shortening. Loss of the first double bond occurs only when it is located in position 4[67, 136].

Nothing is yet known about regulation mechanisms in degradation of unsaturated fatty acids.

7. Biological Functions

Since the feeding experiments of *Burr* and *Burr*[137] in 1929 it is known that some unsaturated fatty acids are essential dietary constituents for the rat. This significant observation was repeatedly confirmed during the following three decades and extended to other animal species. Detailed reviews describe the deficiency symptoms for essential fatty acids[138]. In 1958, unsaturated fatty acids were shown to be "essential" for childen[139]. A few years ago fatty acid deficiency symptoms were established in patients who had been fed parenterally for prolonged periods[140].

It proved to be particularly difficult to detect which unsaturated fatty acids are the essential ones. Studies on the biosynthesis of unsaturated fatty acids (Section 6.1.1) have shown that animal organisms can synthesize oleic acid but not linoleic acid and α-linolenic acid. Hence the desaturases required for introduction of the second and third double bond into the methyl end of oleic acid are missing. If linoleic and/or α-linolenic acid is administered in the diet of an animal organism then it can synthesize the higher members of both fatty acid families by introduction of further double bonds and chain elongation (Section 6.1.3).

If an attempt were made to derive a definition of the term "essential fatty acids" on this basis, then only linoleic and α-linolenic acids would be strictly essential since all other polyunsaturated fatty acids can be synthesized by animal organisms on supply of suitable precursors. However, another approach has been adopted for defining the expression "essential fatty acids" in that the efficacies of the individual acids in counteracting the symptoms of fatty acid deficiency are compared with one another[141]. It was found that administration of acids belonging to the linoleic acid family best dispelled the symptoms of fatty acid deficiency, and the most effective acid was arachidonic acid[142].

To this day it has not been adequately established in which metabolic reactions or in which structural components of the cell the absence of essential fatty acids can initiate pathological changes. However, two topics have recently come to the fore, which could make important contributions to this subject. Unsaturated fatty acids having 20 carbon atoms and three or four double bonds are precursors of prostaglandins[143] (Fig. 16). The physiological properties of the latter are so varied that there are grounds for believing that the relation to the polyunsaturated fatty acids suffices to explain the essential nature of these acids.

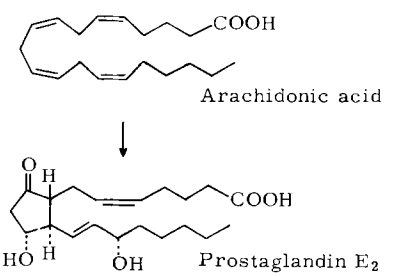


Fig. 16. Formation of prostaglandin E_2 from arachidonic acid.

The second field supplying important knowledge about the biological function of unsaturated fatty acids is membrane biology. As the view is more widely adopted that membranes are not static but dynamic structures whose biological properties depend upon their two fundamental components—proteins and lipids—the membrane lipids and hence also the unsaturated fatty acids continue to attract growing attention.

Judging by their chemical structure, the membrane lipids are extremely heterogeneous[144]. This applies not only to the hydrophilic partial structure but, to an even greater extent, to the hydrophobic part of the molecule, *i. e.* the fatty acid group. The most common membrane lipids are the phospholipids (Fig. 17), which are distinguished from other lipids by their higher content of unsaturated fatty acids[144].

The former view that membrane lipids merely form an apolar phase between aqueous regions and serve as a rigid matrix for biologically active proteins[145] has been modified. Discussions of such varied biological properties of membranes and membrane processes, such as permeability[146], transport properties[147], inhibition of wetting[148], nervous conduction of stimuli[30, 149], enzymatic reactions[150], and the cellular immune reaction[151] assume that they arise from the presence and the physical state of the membrane lipids. The state and transition temperature of reversible phase changes of lipids

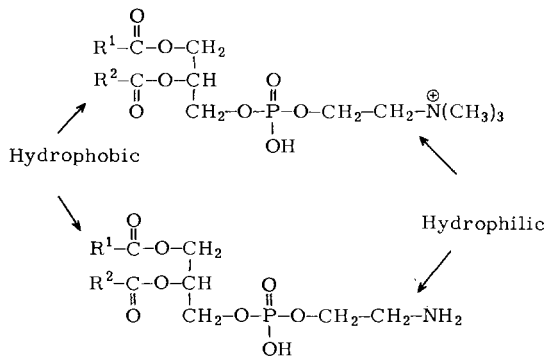


Fig. 17. Structure of the two most frequent phospholipids. Above, phosphatidylcholine (lecithin); below, phosphatidylaminoethanol (cephalin). R^1 and R^2 are long-chain saturated or unsaturated alkyl groups.

are in turn largely determined by the chain length and the number and positions of double bonds in the fatty acids present in the lipids (Section 3).

Reversible phase transitions, as investigated for model membranes[28, 30, 31, 149, 152, 153]—monolayers, bilayers, liposomes—also take place in biological membranes[29-31, 153]. Moreover, preliminary experimental evidence has been obtained that the lipid structure influences the conformation of proteins[154]. It is currently being discussed whether the changes in membrane properties resulting from phase changes of the lipids enable the cell or cell organelles to adapt to changing conditions. Thus it is envisaged that changes in an external parameter promote structural changes in the membrane which in turn lead to a change in function of the membrane[145, 153]. One important task of unsaturated fatty acids in lipids of biological membranes would accordingly lie in the facilitation of reversible phase changes in membrane lipids in the physiological temperature range.

The bewildering heterogeneity of membrane lipids in various types of membranes[144] or even within one membrane was formerly almost uninterpretable, and it was only the relationships sketched out above involving the lipid composition, reversible phase changes, and the "functioning" of a membrane that permitted some understanding of the complexity of membrane lipids.

Viewed from this vantage point, the exceptionally high proportion of highly unsaturated fatty acids—4,7,10,13,16,19-docosahexaenoic acid or 5,8,11,14,17-eicosapentaenoic acid—in the phospholipids of the photoreceptor membrane in the eyes of vertebrates[155] and invertebrates[156] are of particular interest. This fatty acid pattern justifies the assumption that the visual pigment rhodopsin possesses an environment of great mobility[157]. Support for this hypothesis comes from experiments using polarization optical techniques which showed that rhodopsin undergoes rotational movement with a relaxation time of 20 μs in the photoreceptor membrane[158].

Polyunsaturated fatty acids also play a central role in discussions of the pathogenesis and prophylaxis of atherosclerosis[159-161]. This is a significant subgroup of the general degenerative wall diseases of arteries (arteriosclerosis) characterized by development of irregular lipoid deposits (plaques) in the interior layer (intima) of the arterial wall.

The plaques are rich in cholesterol esters[162]. The molecular mechanism of plaque formation has not yet been elucidated. Clinical research has established that atherosclerosis is a multifactorial process[159, 160]. Apart from high blood pressure and smoking, an abnormal increase in blood lipids, especially cholesterol, has been recognized as one of the most significant risk factors.

Today it is universally accepted that polyunsaturated fatty acids reduce the blood level of cholesterol[159-161], and all dietary measures adopted in the prophylaxis of atherosclerosis resort to fats having high contents of these fatty acids. Vegetable oils are particularly suitable for such purposes[160]. However, any conclusions about the origin of excessive cholesterol levels in the blood that may be drawn from such "feeding experiments" should be viewed with great caution[163]. These diets are far too complex for any such interpretations. Apart from the content of saturated and unsaturated fatty acids, other dietary components also have to be considered, *e.g.* cholesterol and vegetable sterols.

8. Conclusion

The past two decades have seen a rapid development in the chemistry and biochemistry of unsaturated fatty acids. Syntheses have been discovered for production of radioactively labeled, highly unsaturated fatty acids in good yields. This was an important requirement for the study of biochemical and biological aspects.

Use of modern analytical techniques has shown that these methods make an important contribution to the structural elucidation of unsaturated fatty acids. Further advances can be expected in the next few years.

The metabolism of unsaturated fatty acids has been examined in general terms. Isolation and characterization of the enzymes involved will provide an insight into the regulation of this area of metabolism.

Especially interesting results may also be expected from membrane biology.

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Sequence Analysis of Polypeptides and Proteins by Combined Gas Chromatography-Mass Spectrometry[**]

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A new method for determining the amino acid sequence of polypeptides consists in initial partial hydrolysis to yield a complex mixture of oligopeptides. After derivatization to enhance its volatility, the mixture is analyzed by combined gas chromatography and mass spectrometry. The sequence of the polypeptide is established by a computer from the identified oligopeptides. So far polypeptides having up to 40 amino acids have been analyzed by this method. The advantages and disadvantages of the new method compared with the stepwise procedure of the Edman degradation are considered. Since the two methods are based on fundamentally different principles they may prove to be complementary.

1. Introduction

Depending upon their origin and function, proteins may have widely differing physical and chemical properties. Largely inert forms of highly insoluble proteins such as keratin or elastin can be contrasted with the extremely sensitive structures of many hormones (*e.g.* glucagon, insulin) and enzymes (*e.g.* ribonuclease A, chymotrypsin) which catalyze a multitude of reactions and regulate the metabolism of living organisms. Furthermore, the molecular weight is subject to wide variation within this class of natural products (*e.g.* insulin, 51 amino acids[1][***]; a polypeptide chain of an immunoglobulin, 576 amino acids[2]) so that hardly any two proteins have the same physicochemical properties although the same structural principles apply to all proteins. Finally, the chemical variety of their twenty constituent amino acids provides further obstacles to a routine analysis of proteins. A knowledge of their structure is an essential condition for elucidation of the mode of action of these molecules.

Even today, 25 years after the introduction of the Edman degradation[3], successful deciphering of the primary structure of relatively large proteins (sequence analysis) is still a difficult task, although automatic "protein sequencers"[4] have reduced the time and sample weight required. Complete sequence analysis of a protein of unknown structure containing, *e.g.* 200 amino acids takes several years. The result, *i.e.* the "sequence", can only be tested by repeating the analysis. A systematic error will necessarily again falsify the sequence. Classical "structural proof" by total synthesis is illusory in this context: syntheses of polypeptides are even more difficult than their analysis.

A more practicable approach than total synthesis is the development of a second independent analytical procedure providing results that can be compared with those of the automated Edman degradation method. This article describes a method of sequence analysis utilizing a combination of three techniques, *viz.* gas chromatography (GC), mass spectrometry (MS), and computer science. We believe that this method complements the Edman degradation in an ideal manner. The Edman approach requires a free amino group at the N-terminus of a peptide; however, precisely those peptides which are blocked at the N-terminal end can be readily analyzed by mass spectrometry. Nor do amino acids prone to decomposition under the conditions of Edman degradation (*e.g.* Ser, Tyr, or Trp) cause any difficulties in the new method. Furthermore, mass spectrometric techniques furnish the complete sequence of a polypeptide whereas the Edman procedure frequently permits only determination of a partial sequence.

We consider the important contribution of the new procedure to lie in the provision of analyses which are independent of Edman degradation, both chemically and as far as apparatus and method are concerned.

This article first considers the general problems of sequence analysis; the principles of the two above mentioned procedures are then compared and their respective advantages and disadvantages weighed up. An account of the requirements and the modern state of sequence analysis by mass spectrometry is followed by a discussion of its application to the solution of various problems encountered in protein chemistry.

2. Problems and Possibilities of Sequence Analysis

2.1. Edman Degradation Procedure

Polypeptides and proteins are chain-like molecules in which α-amino acids are linked together *via* α-amino and α-carboxyl groups. Given such linkage, an amino group remains free at one end of the chain (N-terminus) and a carboxyl group at the other (C-terminus). Since analysis of the overall structure of such macromolecules has so far run into insuperable difficulties—X-ray diffraction on protein crystals is the nearest approach to this ideal yet to be accomplished—indirect methods of sequence analysis have been developed.

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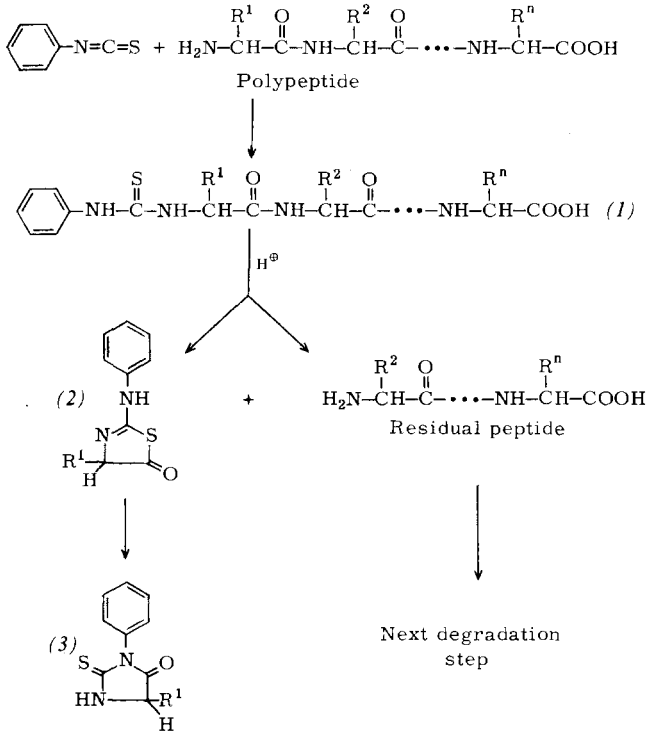
[**] The following abbreviations have been used for amino acids: Gly, glycine; Ala, alanine; Val, valine; Leu, leucine; Ile, isoleucine; Pro, proline; Phe, phenylalanine; Tyr, tyrosine; His, histidine; Trp, troptophan; Ser, serine; Thr, threonine; Asp, aspartic acid; Asn, asparagine; Asx, either Asp or Asn; Glu, glutamic acid; Gln, glutamine; <Glu, 5-oxo-2-pyrrolidinecarboxylic acid; Glx, either Glu, Gln, or <Glu; Lys, lysine; Arg, arginine; Cys, cysteine; Met, methionine.

Other abbreviations: GC-MS, gas chromatography-mass spectrometry; *N*-TFA, *N*-trifluoroacetyl; *N*-PFP, *N*-pentafluoropropionyl; *N*-HFB, *N*-heptafluorobutyryl; OTMS, trimethylsilyl ether; $S_1, S_2, \ldots$, sequence ions in the *N*-TFA, *N*-PFP, and *N*-HFB peptide methyl esters; $A_1, A_2 \ldots$ and $Z_1, Z_2 \ldots$, sequence ions in the polyamino alcohols; M, molecular ion; *I*, retention index; CPI, a potato carboxypeptidase inhibitor; DAP I, dipeptidylamino peptidase I; ng, nanogram (10^{-9} g); pg, picogram (10^{-12} g); OV-17, polymeric methyl (50%) phenyl (50%) silicone oil; Dexsil, polycarborane methyl silicone.

[***] In order to save space citations are often restricted to review articles only.

One such procedure consists in the stepwise liberation of one amino acid after the other—starting from one end of the chain—followed by its isolation and identification. No change may take place in the remainder of the chain since information about its sequence would otherwise be jeopardized. The stepwise consecutive removal of one amino acid at a time from long peptide chains was first accomplished by *Pehr Edman* after numerous trying experiments[3-5].



Scheme 1. Edman degradation.

The "classical" procedure of Edman degradation is shown in Scheme 1. In the first step, the N-terminal amino group of the polypeptide chain is coupled with phenyl isothiocyanate to give the thiourea derivative *(1)*, which is cleaved in a second step. The resulting 2-anilino-5-thiazolinone *(2)* is separated from the shortened polypeptide (residual peptide) and transformed into the 3-phenyl-2-thiohydantoin *(3)* which is identified. The residual peptide can in turn be subjected to the same sequence of reactions, liberating the next amino acid, *etc.* The logical simplicity of the method cannot be improved upon and its successes have been considerable. Thus the overwhelming majority of the polypeptide sequences known today, numbering over 500[6], have been elucidated with the aid of the Edman degradation technique.

However, the most important condition for successful application of this method is the presence of a free amino group at the N-terminus. If it is blocked, as in *N*-acetylated or cyclic peptides, then the peptide cannot be degraded. Furthermore, some amino acids, such as Ser or Trp, are destroyed under the conditions of Edman degradation; Gln can also cyclize under these conditions and thus preclude further degradation. Identification of the liberated amino acid derivatives *(3)* is often also difficult; thus there is no single method suited for all amino acids[7, 8].

Nowadays it is possible to identify between 20 and 40 amino acids, and in exceptional cases over 50, using the protein sequencer developed by *Edman* and *Begg*[4]. However, the degradation reactions cannot be carried on indefinitely since the individual steps do not proceed quantitatively (but in about 96—98% yield) and internal peptide bonds may also be cleaved. In addition, the residual peptide becomes increasingly prone to extraction with the thiazolinone derivative *(2)*, especially when hydrophobic amino acids predominate. Thus in most cases only N-terminal partial sequences but not the entire structures of polypeptides can be elucidated (see Fig. 1). One usually resorts to prior chemical or enzymatic breakdown of the polypeptide into smaller fragments which have to be separated, isolated, and analyzed and whose structure then also provides information about the remaining sequence (at the C terminus) of the polypeptide.

Sequence analysis of a protein thus requires structural elucidation of numerous polypeptides (A, B, C... in Fig. 1), the separation and isolation of the individual polypeptides often being the most difficult and most involved step. Thus, the sequence analysis of thermolysin (316 amino acids) required investigation of 173 fragments[9] and the sequence analysis of a polypeptide chain of IgM immunoglobulin[2] (576 amino acids, the longest chain to have been analyzed so far) required investigation of nearly 600 peptides. A method of sequence analysis which leads not to partial sequences but to complete sequences of polypeptides is therefore highly desirable.

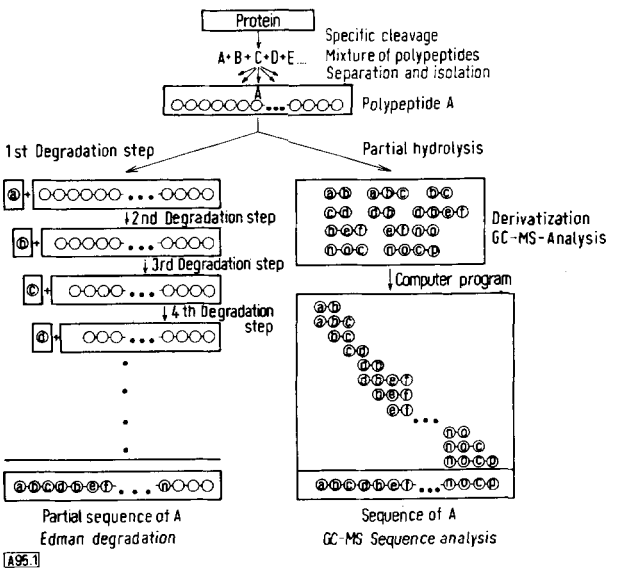


Fig. 1. Schematic comparison of sequence analysis of a polypeptide (A) by Edman degradation and the GC-MS method. Left: The amino acids successively removed by the Edman procedure are identified as derivatives of type *(3)* and lead to a partial sequence of the polypeptide A. Right: Partial hydrolysis of A affords a complex mixture of oligopeptides which is derivatized and identified by GC-MS; the sequence A is assembled from the identified fragments by means of a computer program. Circles marked with small letters symbolize the amino acids identified and the empty circles the unidentified amino acids.

2.2. Gas Chromatography-Mass Spectrometry

The right-hand side of Figure 1 illustrates the principle of the new technique. In contrast to the Edman procedure, the polypeptide A is not shortened in steps, but decomposed into as many oligopeptides with suitable chain lengths as possible by partial acid hydrolysis. All these oligopeptides are identified and the resulting partial sequences combined as in a game of dominos to give the entire sequence A. The

central problem of this method lies in the complete analysis of the very complex hydrolysis mixture which often contains more than 50 oligopeptides. During structural analysis of insulin *Sanger*[11] had to work up such mixtures by chromatography and to isolate and identify the individual oligopeptides, which was an extremely difficult and time consuming task. We have applied combined gas chromatography and mass spectrometry (GC-MS) to the analysis of these mixtures, a technique which permits separation of the components (in the gas chromatograph) and their identification (by the mass spectrometer) in a single experiment[10-13]. A computer is used for collecting and evaluating the extremely high data yield of such a system (GC-MS-computer system).

Sequence analysis with such a system involves four steps:

1) The polypeptide (A in Fig. 1) is split up into oligopeptides. Since all peptide bonds should be represented in these fragments and since the fragments themselves should be of the correct size—di- to hexapeptides which can be analyzed by the GC-MS combination—much depends upon the optimum execution of this reaction step.

2) The mixture of oligopeptides is converted, quantitatively if possible, into the corresponding mixture of volatile derivatives ("derivatization"); the necessary reactions are already performed on a routine basis.

3) The mixture of oligopeptide derivatives is fractionated on a gas chromatography column, the temperature of the column being linearly programmed from 80 to 330 °C. This permits analysis of oligopeptide derivatives having widely differing molecular weights and polarities. The carrier gas is removed before the sample molecules enter the mass spectrometer where they are ionized. We have also standardized this process and can identify derivatives of di- to tetrapeptides, and frequently also of penta- and hexapeptides in a single analytical run. The GC-MS system is controlled by a computer which continually measures the mass spectra (every 5 s). Suitable programs ensure calculation of gas chromatographic and mass spectrometric data (see Section 3.3) and their storage on magnetic tape or microfilm or output *via* a plotter or printout. These data suffice for identification of all oligopeptide derivatives present in the mixture.

4) By means of a computer program the oligopeptides are now joined together according to the "domino principle", yielding the structure of the polypeptide[14] (cf. Fig. 1).

A great advantage of GC-MS sequence analysis compared to sequential degradation methods is that it provides not only an N-terminal partial sequence but the entire sequence of a polypeptide (Fig. 1); the C-terminal part of the macromolecule being identified just as accurately as the N-terminal part. Hence the number of polypeptides (A, B, C ... in Fig. 1) whose structures must be established to deduce the primary structure of a protein should also be reduced.

In addition, the position of each amino acid in the sequence is established not only by a chromatographic parameter (*e.g.* by the R_f value of a colored or fluorescent spot on a thin-layer plate) but above all by the mass spectra of one or several derivatives. Thus the position of the amino acid d Figure 1 is verified by the retention parameters and mass spectra of the derivatives of c-d, d-b, and d-b-e-f. These data are stored permanently on magnetic tape and also on microfilm and can be recalled at any time.

The above GC-MS method is also suited for sequence analysis of peptides with blocked N-termini (see Section 4.2). These peptides can be analyzed without modification, the blocking group being identified at the same time. Nor do amino acids such as Ser, Thr, Trp, which are often decomposed during Edman degradation, cause any difficulties.

3. Conditions for Sequence Analyses of Polypeptides by the GC-MS Method

3.1. Partial Hydrolysis of Polypeptides

The most important method for partial reproducible cleavage of a maximum number of peptide bonds in a polypeptide is *partial acid hydrolysis* (cf. also ref. [1]). A great advantage of this method is that practically all peptide bonds can be cleaved by acid. Under defined conditions (*e.g.* 6 N HCl at 110 °C) there is an optimum hydrolysis time for each polypeptide, after which there is a maximum number of di- to tetrapeptides in the hydrolyzate. Longer hydrolysis times lead to considerable amounts of amino acids, and shorter times to excessively large fragments whose derivatives lack sufficient volatility for identification by the GC-MS method.

A method permitting prediction of this optimum hydrolysis time was therefore developed[15]. For this purpose small samples of the polypeptide are hydrolyzed under widely varying conditions. The resulting mixtures are transformed into *N*-perfluoroacyl peptide methyl esters (see Section 3.2.1) and separated on a gas chromatography column. The amount of oligopeptide derivatives lies in the nanogram range (10^{-9} g) or below. Detection of such small amounts of the fluorinated derivatives was accomplished with the highly selective electron capture detector; even < 1 pg (10^{-12} g) per component can be detected. The optimum hydrolysis time can be deduced from the positions and relative sizes of the peaks.

While all peptide bonds are cleaved by acid, the rates of hydrolysis are subject to wide variation. For instance, a Leu-Leu bond is broken only very slowly owing to steric hindrance by the two isobutyl groups, whereas a Gly-Gly bond is extremely labile. Accordingly, one peptide bond may have undergone quantitative cleavage (*e.g.* Gly-Gly) while another is virtually intact (*e.g.* Leu-Leu). Thus in many cases not all the peptide bonds will be present in the resulting oligopeptide mixture (for example, a Gly-Gly may be absent). This necessitates a second experiment in which the polypeptide is degraded with *enzymes* (with one or several endoproteases such as thermolysin, chymotrypsin, elastase, pepsin, trypsin), usually affording precisely those oligopeptides in good yields which are absent from the acid hydrolyzate. Hitherto, the sum of the oligopeptides identified in the two experiments has always sufficed for determining the structure of the polypeptide under study.

In another novel hydrolytic procedure, a sample of the polypeptide is first degraded by the enzyme dipeptidylaminopeptidase I (DAP I)[16]. This enzyme effects stepwise liberation of dipeptides, starting from the unblocked N-terminus of a peptide. A second sample of the peptide is then shorted by one amino acid by Edman degradation, and the residual peptide subjected to DAP I cleavage. On the basis of the dipeptides identified in the two mixtures, an attempt is then made to establish the structure of the polypeptide. GC-MS is particularly suitable for characterizing such mixtures since dipeptide derivatives are more volatile than derivatives of higher oligopeptides.

However, since only dipeptides are available as fragments, the structures deduced are often rather uncertain in the case of longer polypeptides[17]. A decision between several isomeric sequences must then be reached by supplementary experimentation. Further difficulties arise if the basic amino acids Arg and Lys occupy the N-terminal position or if the polypeptide contains Pro, since these two structural features suppress the activity of the enzyme. We have therefore merely applied these techniques to the structural analysis of relatively small tryptic peptides[18] and to the confirmation of structures determined by other methods[14]. A recent publication has shown[18a] that the inhibitory action of the basic amino acids, but not that of Pro, can be overcome by use of the enzyme dipeptidylaminopeptidase IV; the scope of this hydrolysis method should thereby be enhanced considerably.

3.2. Preparation and Properties of Volatile Peptide Derivatives

The actual analytical process in gas chromatography and also in mass spectrometry takes place in the gaseous phase. The vapor pressure of peptides is, however, too low for these analytical techniques owing to their high polarity and their zwitterionic character. During the past 15 years several research groups have been engaged in the development of peptide derivatives having maximum volatility and displaying mass spectra which permit deduction of the sequence. The "sequence ions"—*i.e.* ions revealing the positions of amino acids in the sequence—should be of high intensity and easily recognizable.

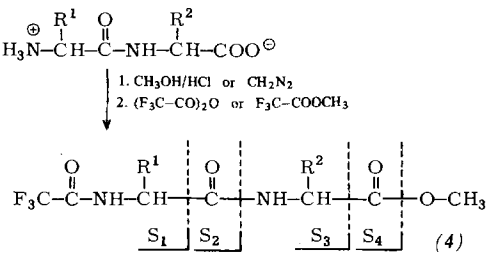
The permethylated peptide derivatives introduced by *Lederer et al.*[19–21] have found wide application; they are prepared by the basic catalyzed action of methyl iodide on *N*-acetyl peptide methyl esters. Although these permethylated derivatives have excellent mass spectrometric properties they usually exhibit inadequate volatility for gas chromatography. The same applies to numerous other peptide derivatives (cf. ref. [22]); they are useful only when pure peptides or very simple mixtures are present and gas chromatography is not required for their separation. However, the sensitivity and time requirement are hardly more favorable than in the classical Edman procedure. Mass spectrometric methods only have a definite advantage in the analysis of peptides having blocked N-termini[23]. Complex peptide mixtures have to be resolved into numerous fractions prior to identification[24].

Three classes of peptide derivative prove to be sufficiently volatile for gas chromatography; their preparation, properties, and applications will be considered in the following sections:

3.2.1. *N*-Perfluoroacyl Peptide Methyl Esters

In 1960, *Weygand et al.*[25] accomplished the first separation of peptide derivatives by gas chromatography, namely *N*-trifluoroacetyl (*N*-TFA) peptide methyl esters *(4)*, which are very easily prepared according to Scheme 2.

The mass spectra of these derivatives[26–29] contain sequence ions formed by cleavage of the peptide chains on both sides of the CO groups with preferential retention of the positive charge in the N-terminal fragment (four ions of this kind, S_1 to S_4, are shown in Scheme 2). These sequence ions are also clearly seen in peptide derivatives having simple (*e.g.* aliphatic) amino acids. The mass spectra of peptide derivatives with trifunctional amino acids are often more difficult



Scheme 2. Synthesis of *N*-trifluoroacetyl peptide methyl esters *(4)*.

to interpret. For instance, the sequence ions S_1 and S_3 are clearly discernable in Figure 2a, whereas the sequence ions S_2 and S_4 appear with very low intensity and are overshadowed by other ions which are of less importance for derivation of the sequence (*e.g. m/e* 162). Verification of the sequence therefore requires recording of high-resolution mass spectra and metastable transitions.

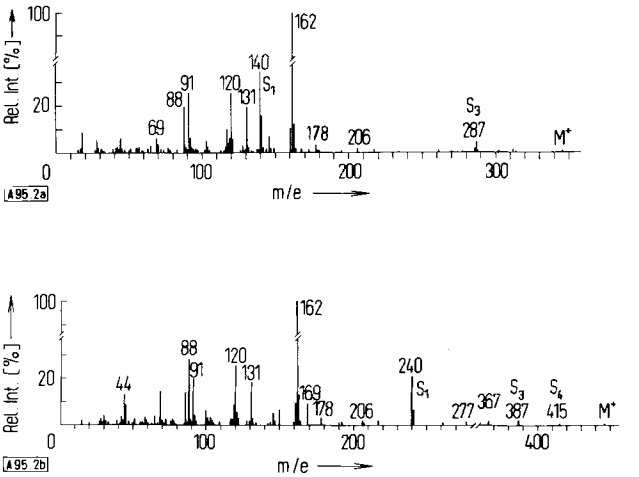


Fig. 2. Comparison of the mass spectra of some Ala-Phe derivatives: a) *N*-TFA-Ala-Phe-OMe *(4a)* [27]; b) *N*-HFB-Ala-Phe-OMe *(5a)* [31]. Fragment ions which cannot be recognized in the formulae *(4a)* and *(5a)* are:

m/e	ion⊕
44	$H_2N{=}CH{-}CH_3$
88	$H_2N{=}CH{-}COOCH_3$
91	C_7H_7 (tropylium)
120	$H_2N{=}CH{-}CH_2{-}C_6H_5$
131	$C_6H_5{-}CH{=}CH{-}C{=}O$
162	$C_6H_5{-}CH{=}CH{-}COOCH_3$

The most important condition for reliable identification of these derivatives is the occurrence and recognition of molecular ions. Molecular ions are easily recognized in mass spectra of pure peptide derivatives; difficulties are sometimes encountered with impure fractions. A number of trifunctional amino acids also had to be transformed in further reactions. Thus amino acids bearing an OH-group in the side chain were *O*-trimethylsilylated; those containing sulfur (Cys, Met) were desulfurated with Raney nickel[28]. *N*-Trifluoroacetyl derivatives *(4)* have so far been mainly employed in the analysis of cyclic peptides[29]; fortunately they contained mainly hydrophobic amino acids which are ideally suited to gas chromatography and mass spectrometry.

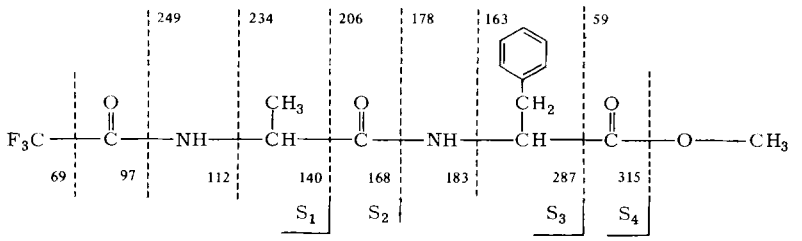
N-Pentafluoropropionyl- (*N*-PFP)[30] and *N*-heptafluorobutyryl (*N*-HFB) peptide methyl esters *(5)*[31], formed by the action of the corresponding anhydrides on peptide methyl esters, show mass spectra closely resembling those of *N*-TFA peptide methyl esters (see Figure 2b). Only the ions of the N-terminal moiety are shifted into a higher mass range because of the greater mass of the perfluoroacyl groups. The enhanced

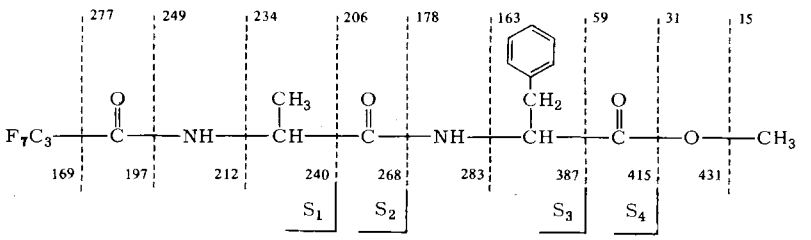
Table 1. Gas chromatographic retention indices (stationary phase: 1% OV 17 [a]) of peptide derivatives [b]. The retention index [42] is a gas chromatographic parameter characterizing the elution of a substance relative to *n*-alkanes; the retention index of $C_{14}H_{30}$ is set at 1400, and that of $C_{22}H_{46}$ at 2200... (see Figs. 7 and 8) (see also Section 3.3).

Peptide	*(4)* TFA... OMe	*(5)* HFB... OMe	*(9)* F_3C-CD_2... OTMS	*(10)* $F_7C_3-CD_2$... OTMS
Ala-Ile	1810	1802	1462	1437
Val-Leu	1853	1842	1538	1506
Leu-Met	2245	2190	1925	1867
Phe-Leu	2320	2271	2030	1965
Tyr-Ala	2548	2484	2185	2117
Met-Met	2575	2501	2273	2200
Phe-Phe	2785	2715	2517	2420
His-Phe	—	3305	2930	2822
Trp-Glu	—	—	3005	2887

[a] On less polar stationary phases, *e.g.* Dexsil 300, the retention indices decrease by 100–300 units.
[b] The retention indices of the *N*-PFP peptide methyl esters lie between those of the the *N*-TFA and the *N*-HFB analogs.

volatility of these compounds represents an advantage over the *N*-TFA derivatives (Table 1). We have therefore tried out the derivatives *(5)* in the structural elucidation of a naturally occurring polypeptide[32] (Section 4.2).





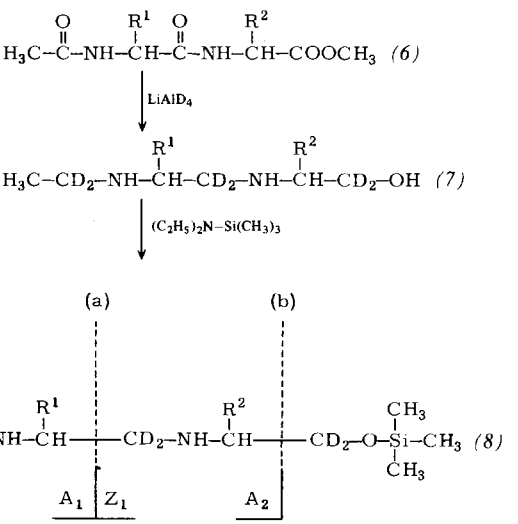
(5a)

3.2.2. Polyamino Alcohol *O*-Trimethylsilyl Derivatives of Peptides

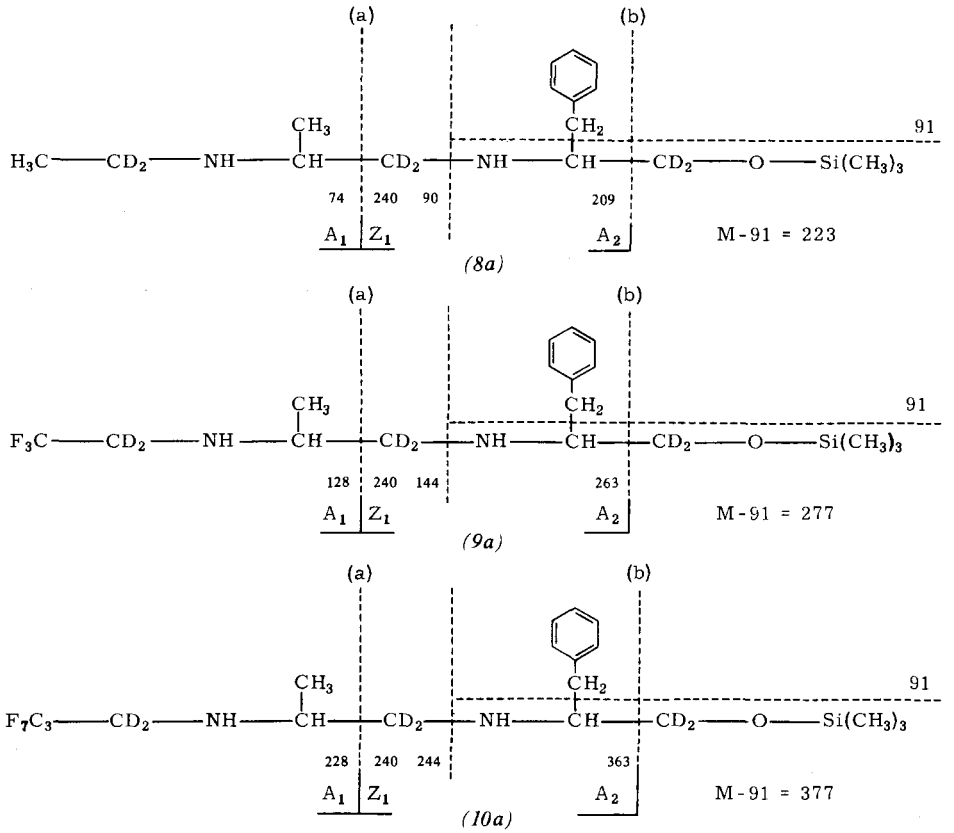
Biemann et al.[33, 34] have proposed a much more radical modification of structure in order to raise the volatility of peptides: all carbonyl groups of *N*-acetyl peptide methyl esters *(6)*—*i.e.* of both the peptide and the ester function—are converted into CH_2 or CD_2 groups by treatment with $LiAlH_4$ or $LiAlD_4$. Since the resulting polyamino alcohols *(7)* still contain free OH groups the method was initially applicable to very simple peptides only. However, transformation of these polar centers into trimethylsilyl ethers affords derivatives *(8)* having properties very suitable for gas chromatography[18].

In addition, the mass spectra of these derivatives are very simple and excellently suited to the elucidation of the amino acid sequence. The derivatives *(8)* no longer contain carbonyl groups and a whole series of fragmentation mechanisms responsible for the complicated nature of the spectra of the derivatives *(4)* and *(5)* no longer appear. The backbone of these compounds consists of ethylenediamine units whose C—C bonds undergo preferential electron impact cleavage; the resulting ions are easily recognized and permit derivation of the sequence ("sequence ions").

Thus cleavage of bond (a) in *(8a)* affords two ions (Fig. 3a). The intense ion A_1 corresponds to the N-terminal amino acid while the less intense Z_1 ion indicates the C-terminal amino acid. Since the masses of the ions A_1 and of the ions Z_1 of all amino acids occurring in proteins are different,



(6) *(7)* *(8)*



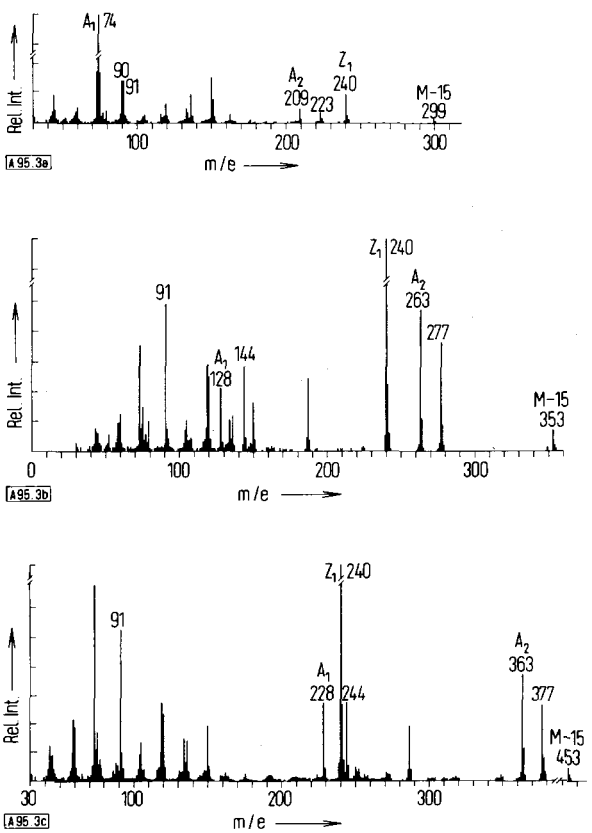


Fig. 3. Comparison of the mass spectra of some polyamino alcohol *O*-trimethylsilyl derivatives from Ala-Phe: a) *N*-dideuterioethyl derivative *(8a)*; b) *N*-trifluorodideuterioethyl derivative *(9a)*; c) *N*-heptafluorodideuteriobutyl derivative *(10a)*.

except for Leu and Ile, the structure of this dipeptide derivative is therefore available. The result can be confirmed by consideration of ion A_2 arising on rupture of bond (b) in *(8a)* and the ion (M − 15) which indicates the mass of the molecular ion, as in all silylated compounds.

The transformation products of longer peptides, *e.g. (8b)*, contain several concatenated ethylenediamine units and thus several C—C bonds subject to cleavage by electron impact (Fig. 4)[18, 35]. The sequences of such peptides can be established in a very simple manner starting from the ion A_1 of the N-terminal amino acid (*m/e* 176 of Thr) *via* the ion A_2 and the higher A ions. This sequence of the peptide is checked by starting from the ion Z_1 of the C-terminal amino acid (*m/e* 251 of Lys) and proceeding *via* the ions Z_2 and Z_3 to Z_4. The (M − 15) ion can also serve as a check. The mass differences between neighboring ions of the A and Z series therefore reveal the individual amino acids and their positions in the sequence.

The principal advantage of this method is that the sequence of a peptide can be built up of readily identified high intensity sequence ions. In contrast, deduction of the sequence of the non-reduced derivatives *(4)* usually requires reliable identification of the very weak molecular ions (see Section 3.2.1).

Peptides containing trifunctional amino acids (including Arg) can also be identified as the derivatives *(8)*. It is, however, a distinct disadvantage that complex His peptides are eluted only as very broad peaks, if at all, from the gas chromatography column; we were therefore compelled to identify these peptide derivatives in an additional experiment by direct evaporation of the sample in the ion source of the mass spectrometer. Only very poor yields were also obtained on derivatization of Gln and Asn peptides. The time consumed by derivatization represents a further drawback. This applies especially to the isolation of the polyamino alcohols *(7)* from the mixture of reduction products, which requires removal of the aluminum salts on an anion exchange column[36].

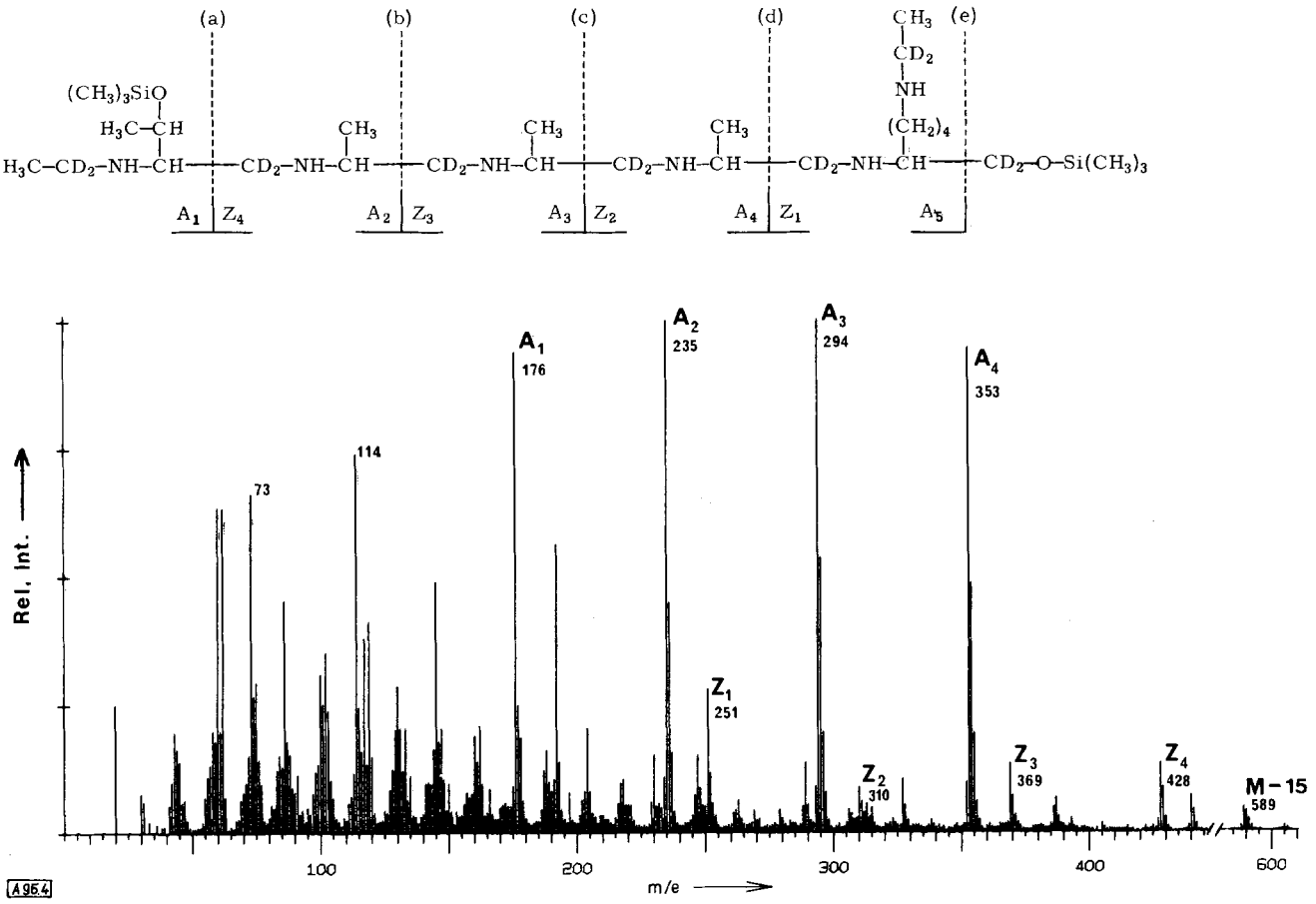
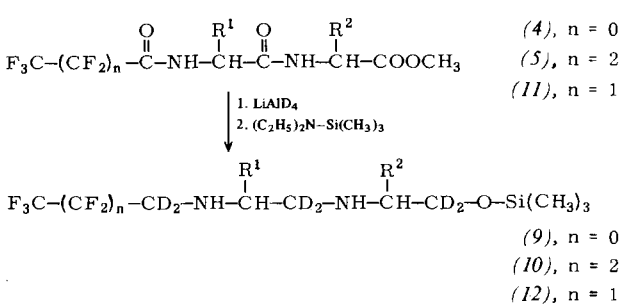


Fig. 4. Mass spectrum of the dideuterioethyl polyamino alcohol *O*-trimethylsilyl derivative *(8b)* obtained from Thr-Ala-Ala-Ala-Lys [35].

3.2.3. Perfluoroalkyl Polyamino Alcohol *O*-Trimethylsilyl Derivatives of Peptides

We have directed much effort to the search for pathways leading to new peptide derivatives displaying improved properties. Such derivatives should be more volatile than derivatives *(8)*, in order to permit identification of larger peptides, and detection of all amino acids including Arg, Gln, Asn, and His by the GC-MS technique. The derivatization reactions should also be simple to perform and the products should be isolable by extraction wherever necessary.

Since the volatility of *N*-acyl peptide methyl esters increases with increasing fluorine content of the acyl group (see Table 1), it appeared an obvious step to further enhance the volatility of the reduced derivatives *(8)*, which are already eluted earlier than the corresponding perfluoroacyl peptide methyl esters, by incorporation of fluorine atoms. Thus, instead of the *N*-acetyl peptide methyl esters *(6)*, their *N*-TFA, *N*-PFP, and *N*-HFB analogs *(4)*, *(11)*, and *(5)*, respectively, were reduced by $LiAlD_4$. The products could be extracted from the reaction



mixture and *O*-trimethylsilylated to give *(9)*, *(12)*, and *(10)* very simply and in high yield (see ref. [37] for experimental methods).

The retention indices of some dipeptide derivatives of types *(9)* and *(10)* are listed in Table 1. These reduced derivatives are considerably more volatile than the non-reduced derivatives *(4)* and *(5)* (the difference in retention indices amounts to 300 to 400 units). The volatility of the polyamino alcohol derivatives and of the *N*-acyl peptide methyl esters increases with increasing fluorine content[37]; thus the derivatives *(10)* are the most volatile peptide derivatives known today.

As the volatility increases, so does the range of peptides whose derivatives can be identified by GC-MS. The upper limit is determined both by the number of amino acids (length of the peptide) and by their polarity; *e.g.* the derivative of hexaalanine is eluted much earlier (retention index 2640) than that of the highly polar tetrapeptide Ala-CMCys-Trp-Asp (retention index 4210) (CM = carboxymethyl). The retention indices can be predicted for the derivatives of all peptides (see Section 3.3).

The mass spectra of the new derivatives *(9)* and *(10)* contain very intense and easily recognizable sequence ions (Fig. 3b and 3c), which are analogous to the sequence ions of the derivatives *(8)*. Fortunately, the intensity of the sequence ions is well balanced, as is shown by comparison of the mass spectra of the non-fluorinated derivative *(8a)* (Fig. 3a) and the fluorinated derivatives *(9a)* and *(10a)* of Ala-Phe (Fig. 3b and 3c, respectively). The mass spectrum in Fig. 3a is dominated by the A_1 ion of the N-terminal amino acid whereas all the other sequence ions have much lower intensities. In

the mass spectrum shown in Figure 3b the A_1 ion is still clearly seen, although much less intense since the electron-withdrawing fluorine atoms lower the basicity of the nitrogen and hence the stability of the immonium ion:

$F_3C{\leftarrow}CD_2{\leftarrow}\overset{\oplus}{N}H{=}CH{-}CH_3$ A_1-ion of Ala

Accordingly, the intensity of all other sequence ions occurring with low intensity in Figure 3a is greatly enhanced. The same applies to the mass spectrum in Figure 3c with the sole difference that the ions containing the N-terminal amino acid (and therefore the perfluoro group) have mass numbers that are 100 units greater. The A ions are thus shifted into a range of higher mass numbers less affected by background or silyl ions and are therefore easily recognized.

Comparison of the mass spectra of the reduced peptide derivatives *(8a)*, *(9a)*, and *(10a)* (Fig. 3) with those of the non-reduced compounds *(4a)* and *(5a)* (Fig. 2) clearly shows how very much the intensity of the sequence ions is increased by the absence of the carbonyl groups; the mass spectra become simpler and easier to interpret. The contribution of the sequence ions to the overall yield of ions in the mass spectra of derivatives *(9)*, *(10)*, and *(12)* usually lies between 30 and 60 %[38]. In contrast, the mass spectrum of the tripeptide *N*-TFA-Val-Ile-Ala-OMe contains only 9 % of sequence ions[39].

The most important advantage of the new derivatives may be seen in the fact that *all* amino acids can now be determined by the GC-MS method. Although Arg-containing peptides give only low yields on derivatization, we have been able to identify these peptides too in the hydrolysis mixtures of naturally occurring polypeptides (Sections 4.1 and 4.2). The Arg-containing peptides can also be modified by hydrazinolysis in good yield prior to derivatization, the strongly polar guanidino groups being converted into amino groups. Peptides containing Cys are *S*-carboxymethylated or *S*-aminoethylated prior to derivatization. These derivatives are superior to the *S*-benzylated derivatives[40] on account of their higher volatility. Finally, peptides containing His can also be derivatized in high yields and determined by GC-MS (see Section 4.2).

Since there is no difference in mass between the side chains of Leu and Ile, the sequence ions of these two amino acids have the same mass numbers. A distinction between Leu and Ile is possible by examining the relative intensities of the sequence ions of the reduced derivatives *(9)*, *etc.*, and of the non-reduced derivatives *(4)*[29], a procedure sufficing for identification of smaller peptides. In the case of complex peptides, the derivatives have to be compared with authentic peptide derivatives.

3.3. Methods of Identification by GC-MS

The mass spectra of suitable peptide derivatives are adequate for identification of pure fractions of a GC-MS experiment (see Section 3.2). However, since partial hydrolysis of polypeptides leads to extremely complex mixtures—often containing 50 and more fragments—all the components of such mixtures cannot be separated on a single gas chromatography column. The fractions leaving the end of the column often comprise several unseparated peptide derivatives. The *mass spectra* of such fractions are therefore made up of fragment ions of several derivatives, which is a serious obstacle to interpretation. In particular, the identification of trace components is frequently impossible.

These trace components can be identified with the aid of *mass chromatograms*[11] (selection ion records) of sequence ions. The mass chromatograms are obtained by plotting the intensities of individual ions *versus* time (or the serial numbers of continuously recorded mass spectra). The maxima in the mass chromatograms of sequence ions thus reveal peptides having a particular amino acid in a particular position of the sequence; *e.g.* the maxima in the mass chromatogram of the A_1 ion of Thr indicate those peptides which contain Thr at the N-terminus.

In Figure 5a we have plotted the total ion chromatogram of a derivatized polypeptide hydrolyzate, and in Figure 5b the mass chromatogram of the ion *m/e* 114. This fragment ion appears with high intensity in the mass spectra of peptide derivatives containing Lys. The maxima in this mass chromatogram indicate the Lys peptides, which can thus be picked out relatively simply from the maze of the mutually overlapping fractions in spite of the complexity of the mixture.

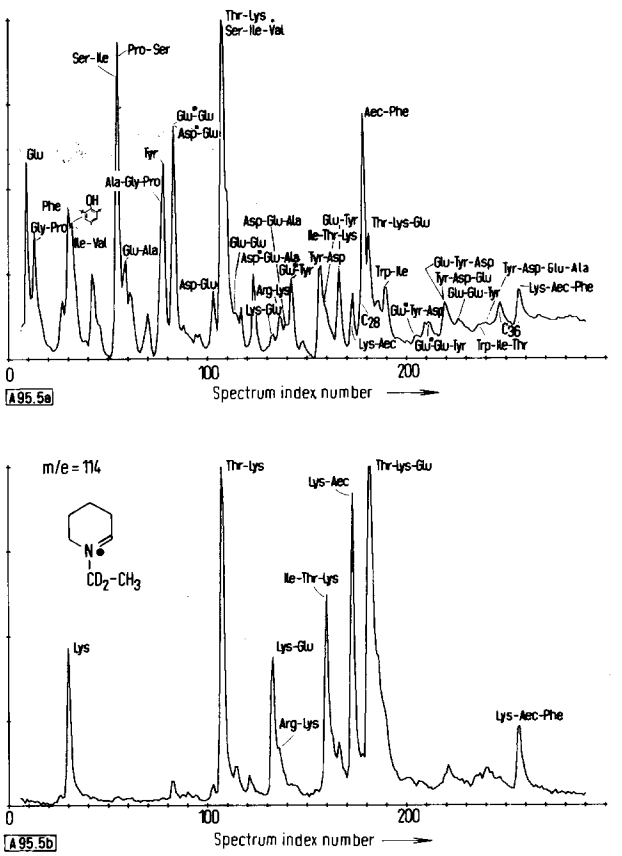


Fig. 5. a) Total ion chromatogram of a mixture of dideuterioethyl polyamino alcohol *O*-trimethylsilyl derivatives of type *(8)*, prepared by partial acid hydrolysis of the eicosapeptide from the C-terminal part of actin [44]; *, identified after elimination of trimethylsilanol; b) mass chromatogram of the ion *m/e* 114. Aec = aminoethylcysteine.

Owing to the chain structure of peptides and peptide derivatives, experience permits prediction of not only their mass spectra but also their gas chromatographic properties[35, 41]. We have chosen the *retention indices*[42] as gas chromatographic parameters; these indices give the positions of the peaks in a gas chromatogram relative to *n*-alkanes introduced with the sample. The parameters are therefore largely independent

of the experimental conditions and hence particularly characteristic.

The retention indices (I) of all polyamino alcohol derivatives can be calculated by simple addition of contributions (Δ) of the individual amino acids. The contribution of the N- and C-terminal groups Δ_t, which decreases with increasing fluorine content (and hence with increasing volatility of the polyamino alcohol derivative) must also be considered:

$$I = \sum_{1}^{n} \Delta_i + \Delta_t$$

The retention indices of two derivatives of type *(8)* are calculated to illustrate the validity of this expression (Δ_t is 735):

I (Tyr-Asp) = 1240 (ΔTyr) + 640 (ΔAsp) + 735 = 2615
I (Ile-Thr-Lys) = 460 (ΔIle) + 535 (ΔThr) + 910 (ΔLys) + 735 = 2640

These calculated values agree well with the measured values (2620 and 2635, respectively), thus confirming the identification of the two peptide derivatives by their mass spectra and mass chromatograms. Calculation of retention indices of fluorinated polyamino alcohol derivatives of very small and very large peptide derivatives required a further correction factor depending upon the size of the derivatives[38]. The resulting values are in good agreement with the experimental data in the broad range between 1400 and 4200.

3.4. Reconstruction of a Polypeptide Sequence from the Oligopeptides

The last step in the GC-MS method of sequence analysis is reconstruction of the sequence of the polypeptide from the oligopeptides resulting on hydrolysis and identified by GC-MS. Reconstruction starts from the N-terminal amino acids (a-b and a-b-c in Fig. 1). Further oligopeptides are then added, thus lengthening the sequence shown in Figure 1 by c-d to give a-b-c-d. To this oligopeptide may be added d-b-e-f, giving the sequence a-b-c-d-b-e-f. The procedure is repeated until the entire structure of the polypeptide has been established. The result can be checked by comparison of the nature and number of the amino acids in this sequence with the result of amino acid analysis of the peptide.

However, it frequently happens that not only one oligopeptide but several can be linked onto a partial sequence. For instance, both b-c and b-e-f can be joined onto the N-terminal oligopeptide a-b (Fig. 1):

a-b + b-c → a-b-c
a-b + b-e-f → a-b-e-f

Two partial sequences result which must be pursued further; each of these sequences can in turn branch further, a feature which greatly complicates the procedure in the case of large polypeptides. We have therefore developed a computer program which performs this stepwise reconstruction automatically[114]. However, an unequivocal result can only be expected if the dipeptides are accompanied by a significant proportion of possible tripeptides and even tetrapeptides. In most cases, a given hydrolysis mixture (*e.g.* an acid hydrolyzate) does not contain all the fragments necessary to unambiguously construct just the one correct sequence, and several isomeric sequences result. A second experiment is then necessary in which hydrolysis is effected by enzymes. The results of the two experiments generally permit deduction of an unequivocal sequence.

4. Examples of Sequence Analysis of Polypeptides by the GC-MS Method

Use of the non-reduced derivatives *(4)*, *(5)*, and *(11)* has already been described in detail[29, 30, 40, 41, 43]. We shall now consider the present state of the art of the GC-MS sequencing method, as illustrated by two examples of sequence analysis of highly complex polypeptides utilizing reduced derivatives of types *(8)*, *(9)*, *(10)*, and *(12)*.

4.1. The C-Terminal Eicosapeptide of Actin

This peptide—the first protein fragment to be identified by GC-MS sequence analysis—was obtained by cyanogen bromide cleavage of actin and contains 20 amino acids. It consists predominantly of trifunctional amino acids, including Arg, His, and Trp which make GC-MS analysis rather difficult. Sequence analysis of this peptide was therefore a realistic test case for the new GC-MS method; above all we wanted to exploit the advantages offered by the direct combination of GC and MS, with the assistance of a computer, and by the peptide derivatives *(8)* which had been developed at that time.

We identified 27 peptides in a partial acid hydrolyzate of this eicosapeptide (Fig. 5a); these species permitted computerized construction of two partial sequences together containing all 20 amino acids (Fig. 6). We then had to link these partial sequences together in the correct manner. The simplest solution to this problem was to determine the N-terminal amino acid (Trp) by conventional methods. All that remained to do was to establish the position of the sole Gln residue which had apparently undergone quantitative conversion into Glu under the conditions of acid hydrolysis. This was also

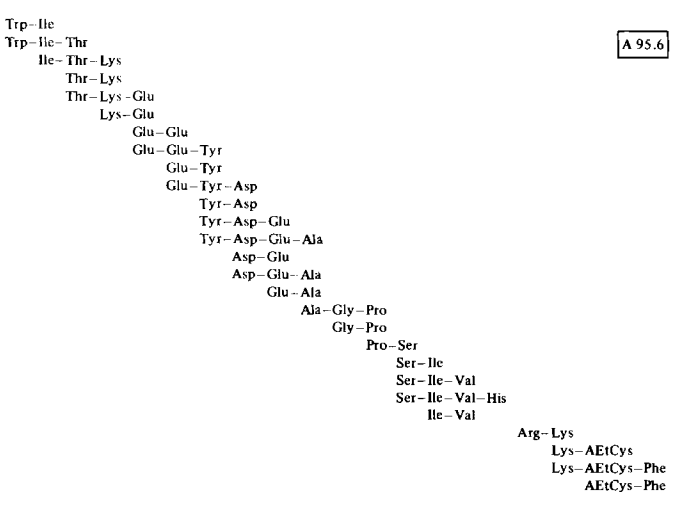


Fig. 6. Stepwise reconstruction of the sequence of the eicosapeptide of actin by overlapping of the oligopeptides identified by GC-MS analysis of a derivatized partial acid hydrolyzate (Fig. 5a) [44]. AEt = aminoethyl.

accomplished in conventional manner—Gln occupies position 5—and the sequence analysis of the eicosapeptide thus concluded[44].

Hence GC-MS analysis of a single hydrolysis mixture of the eicosapeptide and two simple tests for establishing the N-terminal amino acid and the position of the Gln residue were sufficient to determine the complete structure of the polypeptide.

4.2. Potato Carboxypeptidase Inhibitor

This polypeptide contains 39 amino acids—in which all the "difficult" ones are represented—and is by far the largest polypeptide yet to have been analyzed by the GC-MS method. Its analysis enabled us to assess the recently developed derivatives *(9)*, *(10)*, and *(12)*. Since this peptide was also investigated by the automated Edman procedure, we have an opportunity of comparing the two methods.

On starting our investigations we knew that this inhibitor (CPI) apparently consists of a mixture of two polypeptide chains which both possess a blocked N-terminus and differ in the N-terminal regions. We first analyzed the mixture of two peptides obtained by specific cleavage of an Asp-Pro bond from the N-terminal part of the molecule[32]. GC-MS analysis of the derivatized acid hydrolyzate of these two peptides (Fig. 7) revealed a number of oligopeptides including

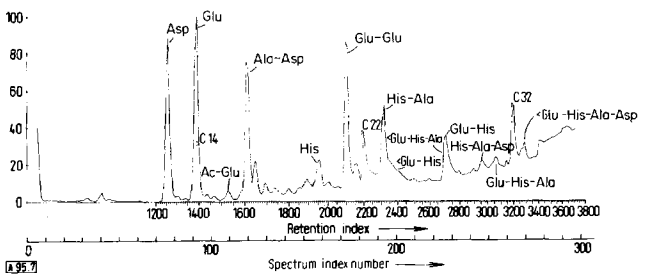


Fig. 7. Total ion chromatogram of trifluorodideuterioethyl polyamino alcohol *O*-trimethylsilyl derivatives of type *(9)* from the partial acid hydrolyzate of the N-terminal part of potato carboxypeptidase inhibitor (CPI) [32].

some containing <Glu (5-oxo-2-pyrrolidinecarboxylic acid) which was thus identified as the blocking group. Overlapping of the peptides listed in Figure 7 yielded the sequence <Glu-Glx-His-Ala-Asx for one of the two peptides. Conventional analyses showed that position 2 is occupied by Gln which is apparently converted into Glu under the conditions of acid hydrolysis. The other peptide was identified as <Glu-His-Ala-Asx in a further experiment. For this purpose the peptide

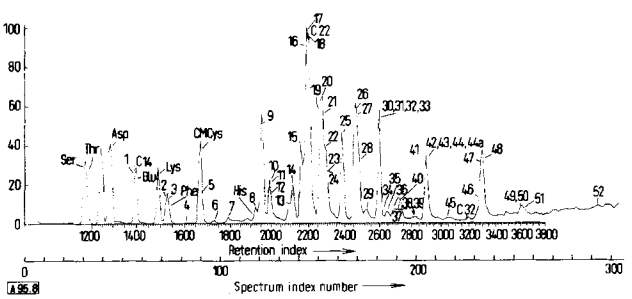


Fig. 8. Total ion chromatogram of trifluorodideuterioethyl polyamino alcohol *O*-trimethylsilyl derivatives *(9)* from the partial acid hydrolyzate of the *S*-carboxymethylated carboxypeptidase inhibitor [38]. The identified peptides are shown with the respective numbers in Fig. 9. 18,34, side products of the derivatization of Ser-Ala-Arg and Pro-Ile-Cys, respectively [38].

mixture was subjected to very brief acid hydrolysis; the resulting peptides were subsequently identified as *N*-HFB peptide methyl esters *(5)* by GC-MS.

It was then explored whether the entire structure of the inhibitor, which consists of a chain of 39 amino acids, could be determined by the GC-MS method. We hydrolyzed a sample of this polypeptide with 6 N HCl and converted the resulting peptide mixture into the derivatives *(9)*. This yielded numerous components which we identified by GC-MS (these peptides are designated by numbers in Fig. 8 and listed in Fig. 9). However, not all peptide bonds were represented

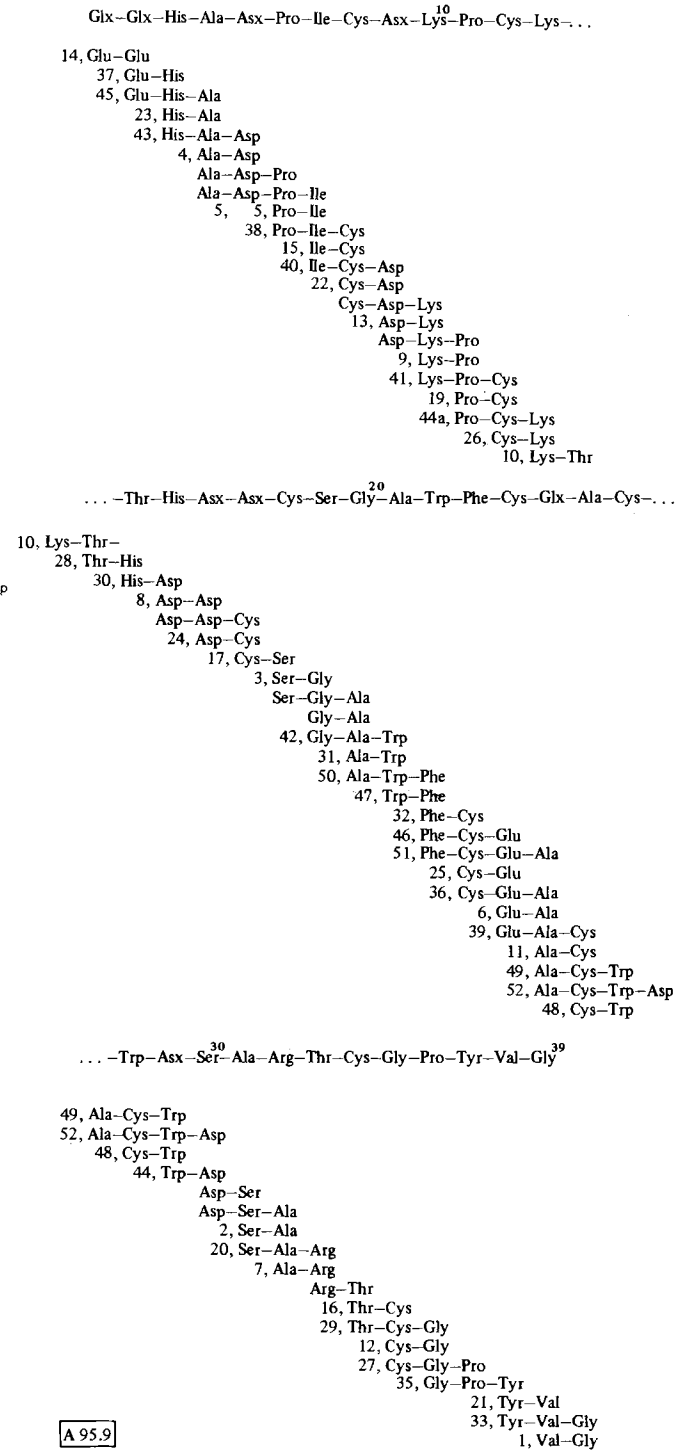


Fig. 9. Stepwise reconstruction of the sequence of the carboxypeptidase inhibitor by overlapping of the oligopeptides identified in the partial acid hydrolyzate (Fig. 8, numbered oligopeptides) and in an enzymatic hydrolyzate (unnumbered oligopeptides) [38].

A: Glu-Glu-His-Ala-Asp-Pro-Ile-Cys-Asp-Lys-Pro-Cys-Lys-Thr-His-Asp-Asp-Cys-Ser-Gly-Ala-Trp-Phe-Cys-Glu-Ala-Cys-Trp-Asp-Ser-Ala-Arg-Thr-Cys-Gly-Pro-Tyr-Val-Gly

B: Glu-Glu-His-Ala-Asp-Pro-Ile-Cys-Asp-Lys-Pro-Cys-Lys-Thr-His-Asp-Cys-Ser-Gly-Ala-Trp-Phe-Cys-Glu-Ala-Cys-Trp-Asp-Asp-Ser-Ala-Arg-Thr-Cys-Gly-Pro-Tyr-Val-Gly

A 95.10

Fig. 10. Result of a computer program [14] for the reconstruction of polypeptide sequences by overlapping of oligopeptides. The oligopeptides of Fig. 9 served as input (without Asp-Asp-Cys).

in the peptides identified; in fact, one each of the highly acid-labile peptide bonds to the amino groups of Ser and Thr had undergone quantitative cleavage. We therefore hydrolyzed a second portion of the polypeptide sample with enzymes which we expected to extensively degrade the polypeptide and yet not completely cleave the important peptide bonds of Ser and Thr. And we did indeed find peptides having these bonds in the derivatized mixture.

All the identified peptide fragments were then overlapped by a computer program to form the structure of the polypeptide. As seen in Figure 10, two possible sequences were obtained which differ in the position of the underlined Asp residue. We therefore sought evidence for the presence of a peptide in the GC-MS data of the two experiments, whose identification would rule out one of the two species. In fact, we found a derivative of Asp-Asp-Cys which had apparently been formed by elimination of trimethylsilanol from the expected derivative and therefore escaped identification. Hence sequence A was verified (Fig. 10).

The new peptide derivatives *(9)* have proved to be of crucial importance in the sequence analysis of this polypeptide since not only Trp and Arg peptides but also His peptides thus become accessible to GC-MS analysis (Figs. 7 and 8). These His peptides had to be identified in an additional experiment in the sequence analysis of the eicosapeptide of actin.

Which of the Glu and Asp residues are present as Gln and Asn, respectively, in CPI could again not be established by the GC-MS method. We do not yet known the reason for these difficulties. Although the Gln- and Asn-containing test peptides could be detected by the GC-MS method, some of these derivatives could only be prepared in low yield. The unequivocal assignment of the Gln and Asn residues is currently under study[*].

The computer program for overlapping of the individual oligopeptides has proved to be of great value; the result of this program (two possible sequences; Fig. 10) required a further interpretation of the GC-MS findings which finally led to the sole possible sequence. The oligopeptides were identified by GC-MS analyses of only two hydrolysis mixtures of the inhibitor.

[*] *Note added in proof* (December 19, 1975): Two techniques for the unequivocal assignment of the Gln and Asn residues are currently under study. First, the polypeptide is modified by diborane (*M. Z. Atassi* and *A. F. Rosenthal*, Biochem. J. *111*, 593 (1969)) *prior* to partial hydrolysis to reduce the free carboxyl groups (of Asp, Glu, and C-terminal residue) to $-CH_2-OH$ groups. The primary amide groups in the side chains of Asn and Gln are not affected by diborane, but are reduced *after* the partial hydrolysis (at that stage, the primary amides are present as carboxyl groups) by $LiAlD_4$ to $-CD_2-OH$ groups. In the final derivatization mixture Asp and Glu can be distinguished from Asn and Gln *via* measurement of the deuterium contents of the derivatives present.

Secondly, we have developed new peptide derivatives which are obtained by permethylation of *N*-acyl oligopeptide methyl esters [*(4)*, *(5)*, *(6)*, *(11)*] and subsequent $LiAlD_4$-reduction and *O*-trimethylsilylation. The primary amide groups of Asn and Gln are transformed into $-CD_2-N(CH_3)_2$ groups leading to derivatives of Gln and Asn with favorable properties.

Let us now consider the conventional sequence analysis of the polypeptide[32]. Although an automatic sequencer was employed, considerable difficulties were encountered. The N-terminal part of the polypeptide could not be identified since the N-terminus is blocked (see Section 2.1). Furthermore, the sequence of the other part of the molecule could only be established with difficulty. Specific cleavage of the polypeptide afforded fragments which were then separated, isolated, and subjected individually to Edman degradation. Some of these smaller peptides were extracted together with the amino acids liberated and were thus lost. Moreover, several gaps appeared in the sequence, due, for example, to the destruction of Ser residues. Complete sequence determination therefore required the painstaking separation, isolation, and structure analysis of several peptides.

5. Outlook

We have repeatedly posed the cardinal question of the optimum peptide derivatives, which play a fundamental role in sequence analysis by the GC-MS method. At present derivatives *(9)*, *(10)*, and *(12)* are superior to all others, being most volatile and exhibiting readily interpretable spectra. In our opinion these derivatives will therefore be generally adopted, although their preparation is more involved than that of the non-reduced derivatives *(4)*, *(5)*, and *(11)*.

A recent comparison of several non-reduced peptide derivatives showed that not even all the dipeptides could be identified in the form of the derivatives *(4)* and *(11)* or the permethylated derivative[45]. We have therefore studied precisely those peptides from which no volatile non-reduced derivatives could be prepared (*e.g.* Trp-Trp) and found that these peptides can easily be converted into the reduced derivatives *(9)*.

And the work involved? Preparation of the reduced derivatives is more time-consuming than that of the non-reduced derivatives but can be performed in routine manner. The data of a GC-MS experiment are recorded automatically by computer but still have to be interpreted manually. However, since the mass spectra and the gas chromatographic parameters of derivatives *(9)*, *(10)*, and *(12)* can be predicted and since all these data are already stored on magnetic tape, automated identification of the peptide derivatives should therefore also be feasible. The only manual step required would then be the injection of the sample of derivatized polypeptide hydrolyzate onto the separating column of the gas chromatograph; recording and interpretation of the data, and reconstruction of the polypeptide sequence by overlapping of the identified oligopeptides (using the existing program) would take place automatically.

Summarizing, it may be said: The peptide derivatives now available and the GC-MS method permit structural elucidation of polypeptides up to 40 amino acids (Section 4); in

the forseeable future it will be possible to analyze even larger peptides. It is, however, an open question whether the structure of proteins—especially those having more than 300 amino acids—can be determined by the above GC-MS method. The resulting mixtures—possibly containing several hundred peptides—might well be completely characterizable. It is, however, hardly likely that a unique possible sequence would result on overlapping of the identified oligopeptides.

Als already demonstrated by *Eck*[46] in his theoretical treatise, more than 336 peptides, including a significant proportion of possible tetra-, penta-, and hexapeptides, are necessary for structural elucidation of a fairly small protein containing 157 peptide bonds. The development of derivatives having higher and higher vapor pressures is therefore of great importance.

However, an alternative approach should lead more directly to the desired goal. The protein should be cleaved specifically, *e. g.* with trypsin or cyanogen bromide, into a few polypeptides (Fig. 1), which are separated and analyzed individually by the described GC-MS techniques. Since these sequences do not overlap, a further sample of the protein should be subjected to a second selective cleavage into a series of other polypeptides which are in turn analyzed by the GC-MS method. The second set of polypeptides permit correct linkage of the first set in a reconstruction of the protein. These linking proteins could also be identified more elegantly by direct GC-MS analysis of suitable hydrolyzates of the complete protein. Such an analysis could be restricted to a search for peptides whose sequences were already represented in the N-terminal and C-terminal part of the polypeptides from the first set. We have already used this direct GC-MS analysis of protein hydrolyzates with success for identification of modified amino acids in enzymes[47].

Recent years have seen various attempts at direct mass spectrometry of peptides—*i.e.* without prior derivatization. Success has been achieved with chemical[48, 49] and photoionization[50]; field desorption[51] has also been used to analyze peptides—even those containing Arg. So far, though, these methods have only been tried with pure peptides; their true value will only become apparent on successful analysis of mixtures. Perhaps high-pressure liquid chromatography could be combined directly with one of the methods mentioned.

I wish to express my sincere gratitude to my teacher and mentor, Professor Klaus Biemann, M.I.T., Cambridge, Mass. Thanks are also due to my former colleagues at M.I.T.—T. R. Smith, J. E. Biller, H.-J. Förster, J. A. Kelly, R. J. Anderegg, and G. Hudson—for their cooperation and numerous stimulating discussions, and to Doz. Dr. J.-H. Fuhrhop and Dr. E. Lustig for valuable comments and suggestions concerning this paper. Financial support from the Federal Ministry of Research and Technology is gratefully acknowledged.

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Unusually High Barriers to Rotation Involving the Tetrahedral Carbon Atom

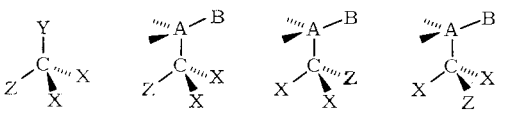
By Michinori Ōki[*]

Rotation about CC single bonds in suitably substituted compounds gives rise to rotational isomers (also called rotamers) which can be isolated if the barrier to rotation is high enough. The present article considers derivatives of triptycene and fluorene whose barriers to rotation are of the order of 30 kcal/mol.

1. Introduction

Restricted rotation about a single bond is an old, yet new field of interest. The classical work by *van't Hoff* and *Le Bel* was criticized from the standpoint that the rotamers predicted by the tetrahedron theory were not isolable. In reply to this criticism, free rotation about a single bond was postulated[1]. It was only in 1936 that the concept of restricted rotation in ethane type molecules was established[2].

According to the theory of rotameric potentials, there are three minima in energy and three rotamers (staggered forms) should be obtainable if the barrier to rotation is high enough to permit their isolation. The simplest example illustrating this concept is a molecule of CX_2YZ type. Although this molecule has no center of asymmetry, it should be resolvable, provided that the barrier is high and either Y or Z which is connected to the central carbon atom *via* a tetrahedral atom does not have threefold symmetry. This applies to the tetrahedrons *(1)*—*(3)* in which −Y has been replaced by ⩾A—B.

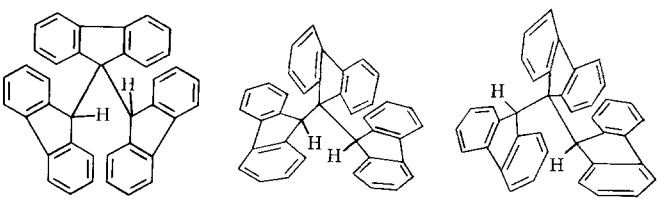


CX_2YZ *(1)* *(2)* *(3)*

(1) has C_{2v} symmetry and is not chiral, whereas *(2)* and *(3)* have no such symmetry and are chiral. If a molecule of CX_2YZ meets these symmetry conditions, it should exist in *meso*, (+), and (−) forms.

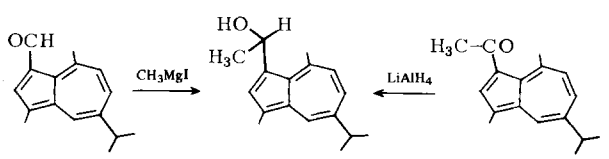
If Y or Z is connected to the central carbon atom *via* a trigonal atom and has no plane of symmetry other than the plane of the triangle itself, there are two stereochemical possibilities. In one case the eclipsed conformation is the stable form and two *meso* forms and two pairs of enantiomers are conceivable. In the other case, the trigonal plane avoids the eclipsed form and at least three pairs of enantiomers are possible.

There are some scattered earlier reports claiming the existence of stable rotamers. As early as 1955, *Suzuki* attributed the existence of two forms of 9,9-bis(9-fluorenyl)fluorene *(4)* to hindered rotation[3] and later assigned the *s-cis,s-cis* and *s-cis,s-trans* structures *(4a)* and *(4b)*, respectively, to these forms on the basis of spectral evidence[4]. However, there are 6 possible rotamers in this compound: one *trans,trans* (*ap,ap*), two *cis,trans* (+*sc,ap* and −*sc,ap*), and three *cis,cis* forms (+*sc*,+*sc* and two +*sc*,−*sc*)[*].



(4) *(4a)* *(4b)*

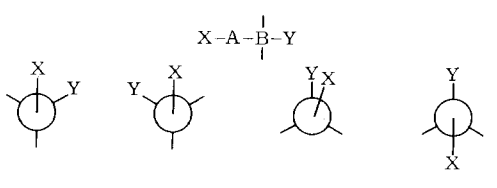
Ukita et al. were able to isolate two forms of compound *(6)*[5]. One was prepared by the reaction of *s*-guaiazulene-1-carbaldehyde *(5)* with methylmagnesium iodide and the other by the reduction of 1-acetyl-*s*-guaiazulene *(7)* with lithium tetrahydridoaluminate. The form prepared by reduction easily deteriorated on heating whereas the other was stable. The authors claimed that the results were best interpreted by assuming the isolation of rotamers: attack by Grignard compound or hydride ion from the least hindered side should produce different isomers.



(5) *(6)* *(7)*

However, a later study on compounds with similar steric properties revealed that the rotational isomer is present in

[*] The symbols *sc* (synclinal), *sp* (synperiplanar), and *ap* (antiperiplanar) used in this article designate the conformation by the torsion angle about an sp^3—sp^2 or an sp^3—sp^3 bond (cf. IUPAC 1968 Tentative Rules, Section E, Fundamental Stereochemistry; J. Org. Chem. *35*, 2849 (1970)). *sc* corresponds to a torsion angle of *ca.* 60°, and + and − indicate the direction of rotation, clockwise and counterclockwise, respectively, of the front atom X required to eclipse the rear atom Y. *sp* and *ap* correspond to the torsion angles of *ca.* 0° and *ca.* 180°, respectively.



Atoms or groups (X and Y) to define the torsion angle are selected according to *R. S. Cahn, C. Ingold,* and *V. Prelog*, Angew. Chem. *78*, 413 (1966); Angew. Chem. Int. Ed. Engl. *5*, 385 (1966).

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The University of Tokyo
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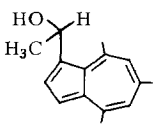
the solid state, at best. ^{1}H-NMR study of *(8)* only showed incipient signal splitting at -70 °C. The room temperature spectra were identical, although several polymorphic forms have been isolated[6]. Even *(9)* only showed line broadening at -25 °C.



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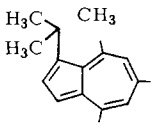
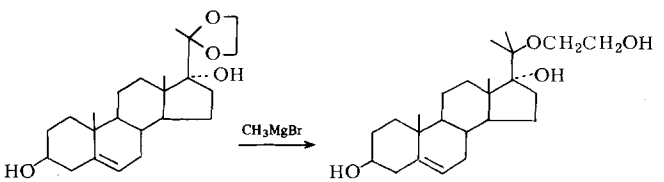


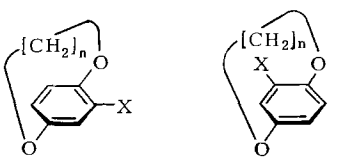
(9)

Kohen et al. treated a steroidal ketal *(10)* with methylmagnesium bromide to obtain two forms *(11)* which exhibited different melting points, ^{1}H-NMR spectra, and optical rotations. They attributed these differences to rotational isomerism[7], but did not equilibrate the isomers. Isolation of the third isomer or equilibration of those isomers would have made the evidence much more convincing.



(10) *(11)*

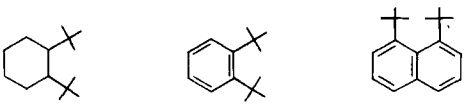
The classical work on optical resolution[8] of [*n*]paracyclophanes and related compounds is a fitting example of rotamer isolation. However, these compounds belong to a different group from those considered in this review in that rotation about multiple sp^3—sp^2 bonds is hindered simultaneously, and they are mentioned only for the sake of completeness. The formula shows some atropisomeric [*n*]paracyclophanes.



In classical work, compounds showing polymorphic behavior were found by accident or were selected by consideration of molecular models. Recent progress in dynamic nuclear magnetic resonance (DNMR), however, has rendered systematic study of the barrier to rotation feasible and permitted prediction of the barrier from available data[9]. The present article surveys this field of chemistry and describes the recent advance of combining DNMR and classical methods in characterizing rotational isomers. Several important aspects of stereochemistry found during the search for stable rotamers will also be described.

2. General Considerations

High barriers to rotation appear to require not only high energy transition states of rotation but also low potential energies in the ground state. A high potential in the transition



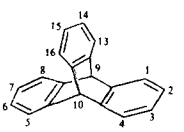
(12) *(13)* *(14)*

state is frequently associated with a high potential in the ground state, but this necessarily lessens the barrier to rotation. Hence, the rather low barriers to rotation in *cis*-1,2-di-*tert*-butylcyclohexane *(12)*[10] 1,2-di-*tert*-butylbenzene *(13)*[11], and 1,8-di-*tert*-butylnaphthalene *(14)* derivatives[12] in spite of the crowdedness in the transition state are believed to be caused by the elevation in the ground state. The low barrier in the azulene derivatives *(6)*, *(8)*, and *(9)* may also be attributed to the same cause.

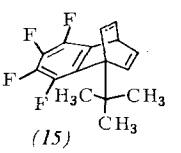
3. Hindered Rotation about sp^3—sp^3 Bonds

3.1. Isolation of Rotamers

An approach to the realization of high barriers to rotation is provided by the triptycenes which can be readily synthesized. Compound *(15)* was found to give two distinct signals in the intensity ratio 2:1 for the *tert*-butyl protons in the ^{1}H-NMR spectrum[13]. The signals began to coalesce at about 120 °C.

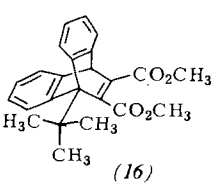


Triptycene

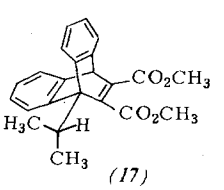


(15)

Although the authors did not mention the barrier to rotation, rough calculation using the chemical shift difference ($\Delta\nu$) and the coalescence temperature (T_c) yielded the free energy of activation $\Delta G_c^{\ddagger}$ at T_c as 20 kcal/mol. Other triptycene-type compounds were also prepared. Compounds *(16)* showed two lines for the *tert*-butyl protons as expected but the ^{1}H-NMR spectrum at 132 °C gave no sign of coalescence or line-broadening, suggesting that the barrier to rotation must be higher than 25 kcal/mol[14]. If we assume the frequency factor A of the Arrhenius equation to be $10^{13}\,s^{-1}$ which is a normal value for internal rotation, then we obtain an activation energy of 23 kcal/mol as the minimum value necessary for isolation of stable rotamers at room temperature (mean lifetime 1 h). Therefore the results with the triptycene analog *(16)* reveal that the steric conditions of this compound meet the requirement for the resolution or isolation of rotamers as stable entities at room temperature.



(16)

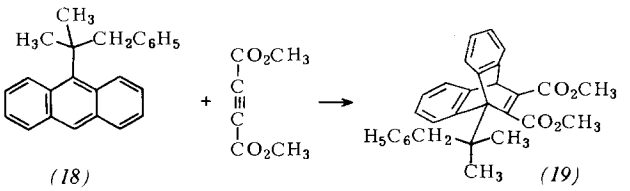


(17)

Since the *tert*-butyl group has threefold symmetry, leading to indistinguishable rotamers, it was replaced by the isopropyl

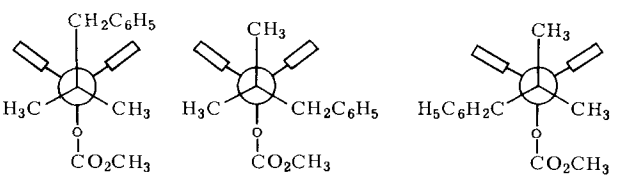
group. However, compound *(17)* could not be resolved into stable rotamers: the activation energy for rotation is only 15 kcal/mol[14].

The results indicate that in order to isolate stable isomers with ethenoanthracene skeleton, the substituent at the bridgehead must be as bulky as the *tert*-butyl group but not have threefold symmetry. Thus compound *(19)* having a benzyl instead of methyl group was prepared[15] by smooth Diels-Alder type addition from *(18)*.



(18) *(19)*

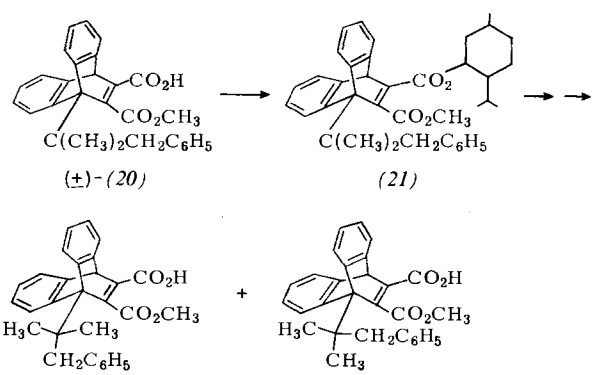
The product gave a ^{1}H-NMR spectrum which exhibited only one signal for the protons of the geminal methyl groups. On heating *(19)* in chlorobenzene, however, increasing amounts of another isomer appear which exhibits two methyl signals and non-equivalent benzyl-methylene protons. These results prove that *(19)* was originally formed by the Diels-Alder reaction in a *meso* form [cf. *(19a)*] which has two methyl groups in equivalent environment. The isomer formed on heating of *(19a)* must be the (±) form [*(19b)* and *(19c)*], because the environments for the two methyls are not equivalent. The nonequivalence of the (diastereotopic) geminal protons of the benzyl group is best interpreted in terms of its proximity to the center of asymmetry.



(19a) *(19b)* *(19c)*

meso or *ap* (±) or ± *sc*

The various rotamers of *(19)* were hydrolyzed to a monocarboxylic acid whose structure is tentatively given as *(20)* because hydrolysis of this compound hardly proceeded further. Resolution of (±)-*(20)* was carried out through crystallization of its (−)-menthyl ester *(21)*. Thus, all three possible rotamers of *(20)* are isolated as stable entities at room temperature

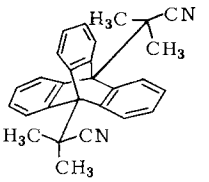


(±)-*(20)* *(21)*

(+)-*(20)* and (−)-*(20)*

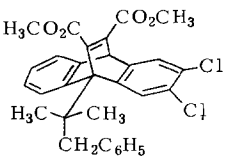
and possess the following characteristics: *meso-(20)*, m. p. 223—225 °C; (+)-*(20)*, m. p. 188—190 °C, $[\alpha]_D^{32}$ +24.8 ($CHCl_3$); (−)-*(20)*, m. p. 188—190 °C, $[\alpha]_D^{32}$ −24.6 ($CHCl_3$)[16].

After the successful separation of isomers of *(19)*, a few subsequent papers reported similar results. *Iwamura* was able to isolate C_2 and C_{2v} forms of *(22)*[17], and *Yamamoto* and *Ōki* reported the isolation of three rotameric forms of *(23)*[18] by chromatographic separation. The latter compounds correspond to diastereomers, although they have only *one* asymmetric carbon atom.



(22)

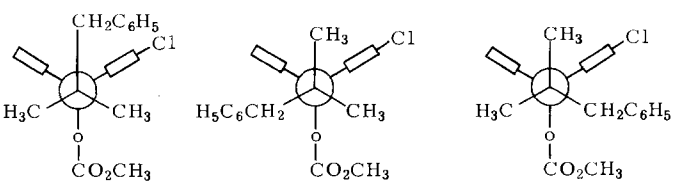
only C_{2v} form shown



(23)

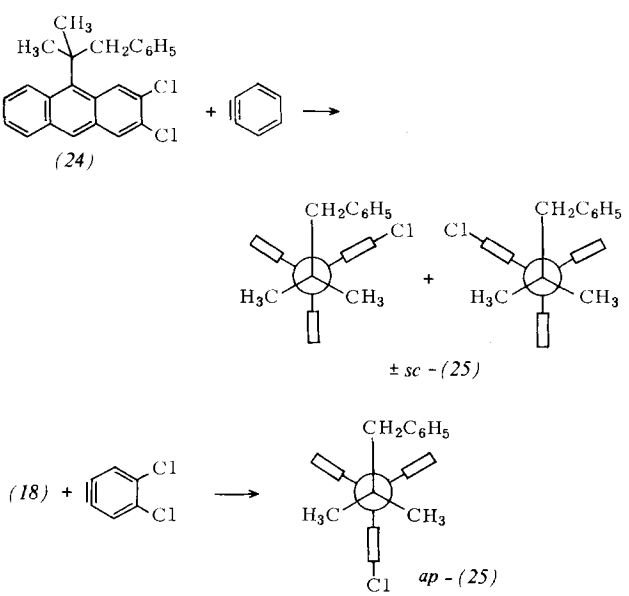
only *ap* form shown

Noteworthy in this context is the stereoselective formation of *(23)*, as already observed in the preparation of *(19)*. Diels-Alder reaction of compound *(24)* with dimethyl acetylenedicarboxylate gave only the *ap* form *(23a)*. The other isomers *(23b)* and *(23c)* were separated after equilibration.



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

Using this technique, it was possible to synthesize ±*sc* and *ap* forms of 2,3-dichloro-9-(α,α-dimethylphenethyl)-triptycene *(25)* separately[19]. Reaction of *(18)* with 4,5-dichlorodi-



(24)

±*sc*-*(25)*

(18) +

ap-*(25)*

dehydrobenzene gave the *ap* form [*ap-(25)*], whereas that of *(24)* with didehydrobenzene produced ±*sc-(25)* only.

3.2. Influence of the Bridging System on the Barrier

Some of the highest barriers to rotation about CC single bonds found in the literature are summarized in Table 1.

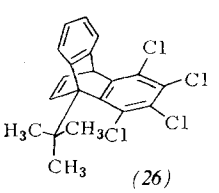
Table 1. Some of the highest barriers for internal rotation.

Compound	E_a [kcal/mol]	log A	Ref.
(19)	33.2	13.3	[16]
(22)	37.7	13	[17]
(25)	33.6	11.7	[19]

The half-lives of these compounds exceed a thousand years at room temperature; hence the rotamers are extremely stable at ambient temperature.

The triptycene skeleton seems to be ideal for exhibiting the high barrier to rotation: in the ground state, the methyls in the *tert*-butyl group reside comfortably between the three benzene rings and yet the transition state is of very high energy because of severe steric interaction.

The barrier should be lessened on replacing the benzeno bridge by an etheno bridge, as was the case for compound *(19)*. However, a Diels-Alder adduct *(26)* prepared from 1-*tert*-butylnaphthalene and tetrachlorodidehydrobenzene did not show any line broadening at 200 °C[20], indicative of a barrier to rotation exceeding 25 kcal/mol. Thus apart from any additional enhancement by the tetrachlorobenzeno group (see Section 3.4), the ethenoanthracene skelton itself is seen to give a high barrier.



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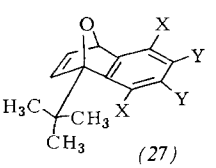


(27)

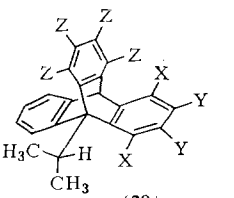
However, replacing the benzeno bridge in *(26)* by an epoxy bridge decreases the barrier to rotation. The methyl signals of compounds *(27)* are sharp singlets at room temperature, whereas they gradually broaden and finally separate into three signals of equal intensity at low temperatures. Total line shape analysis with use of a modified Bloch equation gave satisfactory results and the kinetic parameters were obtained as shown in Table 2[21]. Apparently the barriers are affected by the substituents X and Y on the benzene ring, although only to a limited extent. The type of the bridge seems to be of the prime importance in determining the height of the barrier to rotation.

Table 2. Kinetic parameters for rotation of the *tert*-butyl group in *(27)* (at 25 °C).

Substituent X	Y	$\Delta G^{\neq}$ [kcal/mol]	$\Delta H^{\neq}$ [kcal/mol]	$\Delta S^{\neq}$ [e.u.]	E_a [kcal/mol]
H	H	9.9 ± 1.0	7.1 ± 0.6	− 9.4 ± 2.3	7.7 ± 0.6
CH_3O	H	11.4 ± 1.0	10.2 ± 0.5	− 4.1 ± 1.0	10.8 ± 0.5
F	F	11.1 ± 1.0	7.6 ± 1.0	−11.8 ± 1.0	8.2 ± 1.0
Cl	Cl	12.0 ± 0.9	10.1 ± 0.6	− 6.5 ± 1.0	10.7 ± 0.6
Br	Br	11.1 ± 0.8	12.4 ± 0.4	4.5 ± 1.6	13.0 ± 0.4

3.3. Effect of Bridgehead Substituents

The sharp decrease in barriers to rotation on going from *tert*-butyl to the isopropyl group is worthy of note. Particular interest therefore attached to the combined effect of the bridgehead substituent and the bridge substituent, since the latter can raise the barrier by several kcal/mol.



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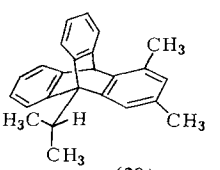


(29)

Table 3. Kinetic parameters for rotation of the isopropyl group in *(28)* (at 25 °C).

Substituent X	Y	Z	$\Delta G^{\neq}$ [kcal/mol]	$\Delta H^{\neq}$ [kcal/mol]	$\Delta S^{\neq}$ [e.u.]	E_a [kcal/mol]
CH_3	H	H	21.8 ± 1.1	17.2 ± 1.4	1.5 ± 1.7	22.0 ± 0.7
CH_3O	H	H	23.6 ± 1.9	21.4 ± 0.7	3.9 ± 2.7	25.4 ± 1.1
Cl	Cl	H	25.5 ± 2.3	30.1 ± 1.4	15.5 ± 2.3	30.7 ± 1.4
Br	Br	H	> 26			
Cl	Cl	Cl	> 26			

Being the second largest alkyl group in the series $(CH_3)_nC_{3-n}$, the isopropyl group is able to induce a high barrier to rotation if the effect of substituents at the bridging system predominates. The barriers to rotation of compounds *(28)* were therefore examined. Total line shape analysis gave satisfactory agreement with the modified Bloch equation. The results are summarized in Table 3[22].

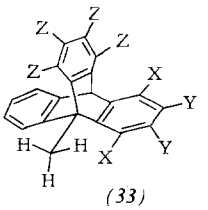
Apparently the barrier is lowest (E_a = 19.9 kcal/mol) for a compound *(29)* which has no substituent in a *peri*-position[*]. However, the barrier is still higher than that in compound

[*] In triptycene, the term *peri*-position should be taken to mean the positions: 1,8; 1,13; 4,5; 4,16; 5,16 and/or 8,13.

(17) (E_a = 15 kcal/mol), again showing that the barrier is higher for the triptycene skeleton than for the etheno-bridged anthracene skeleton. The barrier is surprisingly high when one or two benzeno bridges carry substituents (*e.g.* halogen). It must therefore be possible to isolate stable rotamers of tetrabromo and octachloro compounds at room temperature but no such attempt has yet been reported.

The ethyl group comes next to the isopropyl group in the alkyl series but there seems to be no report on hindered rotation of this group, probably because of the complexity of analysis of the PMR spectra. Instead, some investigations on substituted methyl groups have been performed. The first such publication was authored by *Sergeyev et al.*[23], who observed the coalescence-splitting phenomenon of the *peri*-proton signals of 9-chloromethyltriptycene *(30)*. The barrier was later recalculated to be 13 kcal/mol[24] using ^{13}C-NMR data.

Soon after this finding, it became clear that substituted 9-methyltriptycenes *(33)* give clearer freezing of the rotation[30]. Those which have a halogen substituent in a *peri*-position give separate signals in the intensity ratio of 2:1 for the methyl protons at low temperatures, whereas those with halogens in two *peri*-positions to the methyl group give distinct AB_2 type signals at low temperatures. The barriers obtained are listed in Table 4. *Anderson* reported separation of a methyl signal of compound *(34)* at low temperatures[31].



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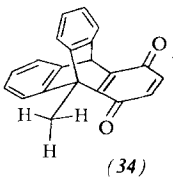
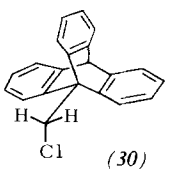


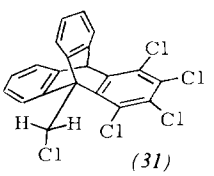
(34)

Table 4. Kinetic parameters for rotation of the methyl group in *(33)* (at 25 °C).

Substituent X	Y	Z	$\Delta G^{\neq}$ [kcal/mol]	$\Delta H^{\neq}$ [kcal/mol]	$\Delta S^{\neq}$ [e.u.]	E_a [kcal/mol]
CH_3	H	H	<8			
CH_3O	H	H	<8			
Cl	Cl	H	10.3±1.0	8.6±0.4	−5.9±2.1	9.2±0.4
Br	Br	H	10.2±1.0	9.6±0.4	−2.1±2.0	10.2±0.4
Cl	Cl	Cl	10.6±1.0	13.5±0.6	9.8±3.0	14.1±0.6
Br	Br	Cl	11.4±0.6	12.4±0.3	3.4±1.3	13.0±0.3
CH_3	H	Cl	11.2±0.7	12.1±0.3	3.0±1.4	12.7±0.3

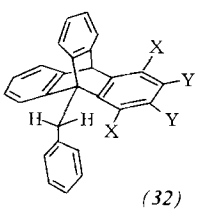


(30)



(31)

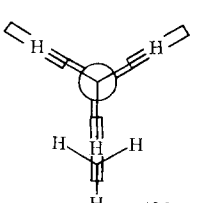
Suzuki and *Ōki* treated a similar compound bearing a chloro substituent at a *peri* position but unfortunately the population was so one-sided that it was not possible to determine the barrier[25]. The barrier to rotation of 9-benzyltriptycenes *(32)* has been roughly estimated to lie in the range of 10—18 kcal/mol[26].



(32)

Methyl, being the smallest alkyl group, is expected to give the lowest barrier to rotation. Indeed, there have been scattered attempts to freeze the rotation of methyl groups; however, the sole evidence obtained consists in line-broadening[27, 28] and one can argue that the broadening may be caused by reasons other than slow rotation. Unambiguous evidence of freezing of the rotation of methyl groups has been presented for the epoxynaphthalenes *(27)*. Their ^{1}H-NMR spectra showed not only broadening of the signals but an unsymmetric line shape at low temperatures[21, 29].

Although the barriers to rotation of the methyl groups of 1,4-dimethyl- and 1,4-dimethoxy-9-methyltriptycenes were too low to be obtained accurately, it was still clear that the barrier for the 1,4-dimethoxy compound is higher than that in the corresponding dimethyl compound. This is an unusual phenomenon, because the van der Waals radius of the methyl group is larger than that of the methoxy group and it is usually thought that the transition state is governed by the steric repulsion between groups concerned. However, this phenomenon is not only found in the methyltriptycenes but also in the isopropyltriptycenes (cf. Table 3). One of the possible explanations for these unusual phenomena is the cogwheeling arrangement of the methyl groups [cf. *(35)*]. It may be argued that it is not the cogwheeling but the raising of the ground state that is responsible for lessening the barrier. However, the high barriers of the bromo compounds contradict this hypothesis: the bromo group should induce a similar barrier to the methyl group, being of almost the same size.



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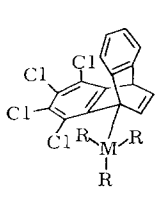


(36), M = Si, Ge, Sn
R = CH_3

If the central carbon atom of the *tert*-butyl group in *(26)* is replaced by other Group IV elements, the barrier shows a considerable decrease[20]. Elongation of the bond is shown by molecular models to cause more severe overlap with the

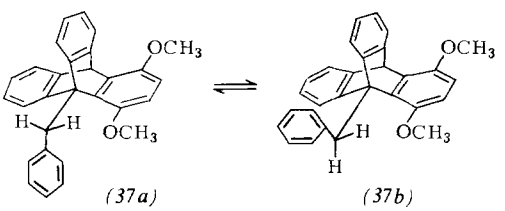
peri-substituent. The decrease in the barrier actually observed is attributed to the easier deformation of the bond angle on descending the Periodic Table.

3.4. Population of Rotamers in Highly Crowded Systems

Population of rotamers in the substituted triptycenes poses another interesting problem. Among 9-isopropyltriptycenes *(28)*, those which have a substituent in a *peri*-position to the isopropyl group exist solely as (±)-forms: no *meso* form was detected even at elevated temperatures. In sharp contrast, 10-isopropyl-1,3-dimethyltriptycene *(29)*, which has no substituent in a *peri*-position, exists as a 2:1 mixture of the (±)- and the *meso* forms, the ratio being the statistical one. Thus the population of the rotamers is regulated by the substituent in a *peri*-position and the type of interaction is repulsive[22]. That only the *meso* form of 1,2,3,4,5,6,7,8-octachloro-9-isopropyltriptycene is known accords with this finding, because the steric repulsion can be minimized in that conformation.

The situation with 9-benzyltriptycene derivatives is in sharp contrast[25]. Especially noteworthy is the case of 9-benzyl-1,4-dimethoxytriptycene which exists as a 2.8:1 mixture of (±) [*(37a)* and its mirror image] and *meso* [*(37b)*] isomers at −40 °C, the ratio being greater than the statistical one in spite of the fact that the (±) form is disfavored by steric effects. Introduction of an electron-withdrawing substituent into the *para* position of the benzyl group enhances the stabilization of the (±) form, whereas an electron-donating substituent has the opposite effect.

9-Chloromethyl-1,4-dimethoxytriptycene exists almost exclusively as the *meso* form.

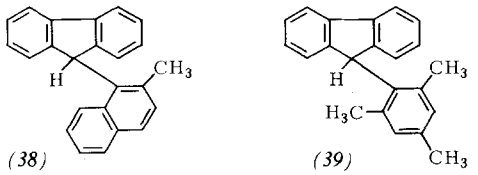


(37a) *(37b)*

This unexpected equilibration was attributed to a charge-transfer type attractive interaction between the substituted benzene rings and the benzene ring of the benzyl group. It seems that the attractive interaction operates between groups of closest proximity if an electron-accepting orbital is available at relatively low level, while the interaction is repulsive if this condition is not fulfilled.

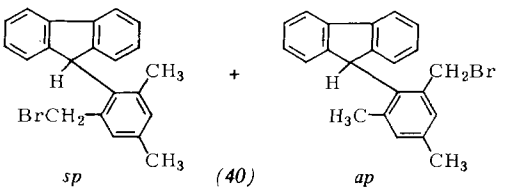
4. Hindered Rotation about sp^3—sp^2 Bonds

Three groups of investigators reported almost simultaneously that 9-substituted fluorene could have high barriers to rotation about the single bond leading to the substituent [32–34]. *Siddall* and *Stewart*[34] were able to concentrate one rotamer of 9-(2-methyl-1-naphthyl)fluorene *(38)* up to >90% purity and another to 58% purity by fractional crystallization. The free energy of activation was found to be 29.2 kcal/mol at 116 °C. They and *Rieker* and *Kessler*[33] pointed out that 9-mesitylfluorene *(39)* could have a barrier to rotation of over 26 kcal/mol from the observation that the signals of the protons of the methyl groups in positions 2 and 6 did not coalesce even at 200 °C.



(38) *(39)*

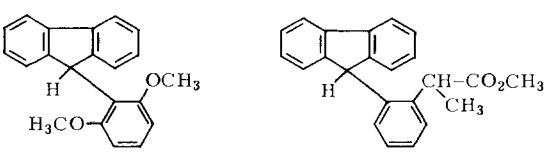
Nakamura and *Ōki*, making use of the DNMR results cited above, succeeded in isolating the pure rotamers of this type, after bromination of compound *(39)* with *N*-bromosuccinimide[35]. The barriers to rotation in compound *(40)* for *sp*→*ap*



sp *(40)* *ap*

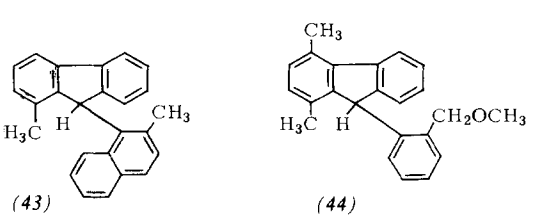
and *ap*→*sp* are almost the same at 27 kcal/mol, the frequency factor being *ca.* $10^{11}\,s^{-1}$. They also succeeded in isolating *sp* and *ap* isomers of 9-(2-methoxy-1-naphthyl)fluorene, the melting points being 125.0—126.0 °C and 121.0—122.0 °C, respectively[36]. The activation energies for the rotations of this compound were found to be rather low, *i.e.* 25 kcal/mol and 24 kcal/mol for *sp*→*ap* and *ap*→*sp*, respectively.

In order to have rotation barriers high enough for isolation of rotamers, it seems necessary to have bulky substituents in positions 2 and 6 of the 9-aryl group. Even 9-(2,6-dimethoxyphenyl)fluorene *(41)* is known to have only 20.6 kcal/mol free energy of activation and compound *(42)* to possess only a low barrier, the coalescence temperature being 60—100 °C for all the signals at 60 MHz[37].



(41) *(42)*

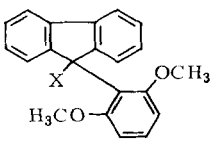
Introduction of a methyl group in position 1 of the fluorene nucleus appears to raise the barrier considerably. Thus compound *(43)* was isolated in two forms (m.p. 152—153.5 °C and 189—191 °C) and the free energy of activation at 166 °C was estimated to be 33.3 kcal/mol[38]. However, this methyl group is not sufficient to permit isolation of fluorene rotamers whose 9-aryl groups are *ortho* substituted. *(44)* is reported to have a free energy of activation of 19.4 kcal/mol at 104 °C[39].



(43) *(44)*

Elevation of the ground state energy has a profound effect on the barriers to rotation of fluorene derivatives. Replacement of the atom in position 9 by hydroxy or chloro group considerably lowers the barrier[32, 33]. The value of E_a is lowered from 19.4 kcal/mol (X=H) to 14.4 (X=OH) and 9.2 kcal/mol (X=Cl). A similar situation is found for triptycene derivatives. 9-Aryltriptycene derivatives *(46)* show a barrier of only 13—14 kcal/mol in spite of the fact that the 9-alkyltriptycenes showed remarkably high barriers[40].

This pronounced effect must be attributed to the rise in ground state energy because of the proximity of the 9-aryl groups to one of the benzeno bridges.



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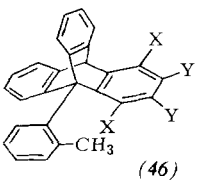
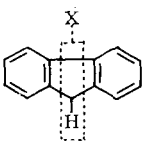


(46)

The mechanism of exchange, observed by ^{1}H-NMR spectroscopy either as a change in line shape or as a decrease or increase in line intensities after isolation of rotamers, might not be a simple internal rotation, especially when the barrier is high. *Ford et al.* carried out a series of experiments to establish the pathway of isomerization of *(43)* and found that the mechanism of exchange between isomers is indeed internal rotation[38].



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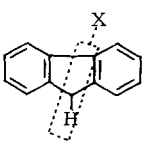

(48)

only *ap* forms shown

Finally, there is the problem of the conformation of fluorenes of type *(38)—(45)*. If they exist in the eclipsed form *(47)*[*], the above cases are examples in which all the possible *meso* rotamers were isolated. However, if the non-eclipsed form *(48)* applies, there are still possible rotamers to be isolated. The latter is believed to be the case because, on lowering the temperature, the signal of the bromomethyl protons of compound *(40)* show a tendency to split into an AB quartet[41]. The phenomenon can only be interpreted by assuming the presence of a chiral center. Thus the enantiomers of 9-arylfluorene undergo rapid interchange at room temperature, whereas the isomerization between *ap* and *sp* forms is slow.

[*] The formulation of the other eclipsed arrangement is unreasonable because the steric effect is unfavorable and the methylene protons of *(40)* do not show diastereotopy in the ^{1}H-NMR spectra recorded in various solvents at room temperature.

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Oxidation-Reduction Condensation

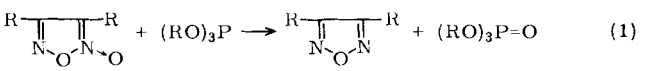
By Teruaki Mukaiyama[*]

This review is concerned with syntheses which can be carried out in the absence of acids and bases. In the case of condensations, *i.e.* the union of two or more reaction partners with elimination of simple molecules such as H_2O or NH_3, the combination of a weak oxidizing agent with a weak reducing agent has proven useful. A particularly suitable reagent for condensations with elimination of water is triphenylphosphane/di(2-pyridyl)disulfane. The phosphane takes up the oxygen atom and is converted into the phosphane oxide, while the disulfane reacts with the two hydrogen atoms to form pyridinethione. Oxidation-reduction condensations have been utilized for the preparation of, *inter alia*, esters, peptides, nucleotides, and macrolides.

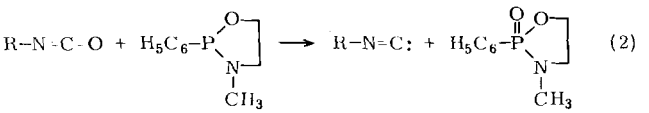
1. Introduction

Ever since strong bases such as alkyllithium compounds became relatively easily accessible, numerous useful syntheses have been developed in which the chemistry of organosulfur derivatives, dianions, alkylcopper compounds or related species plays an integral role. In the case of acids, the discovery of super acids has made it possible to generate synthetically useful carbocations, and Lewis acids[1] have provided the organic chemist with a means of performing numerous versatile syntheses. In the following, we are not concerned with reactions involving strong bases and strong acids but rather with syntheses which are performed in the presence of weak oxidizing agents and weak reducing agents ("oxidation-reduction condensation").

Organic compounds containing trivalent phosphorus, such as trialkylphosphites and trialkyl- or triarylphosphanes can readily take up an oxygen atom and are therefore frequently used as reducing agents, as is illustrated in equations (1)–(4)[2–4].



(1)



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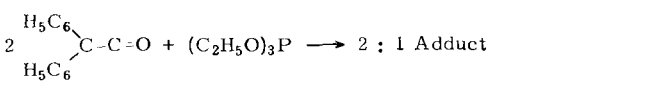

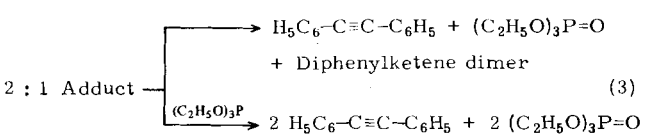

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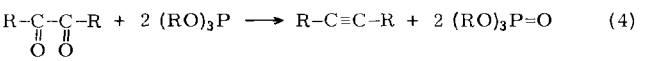
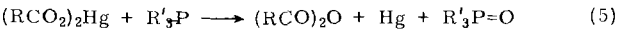


(4)

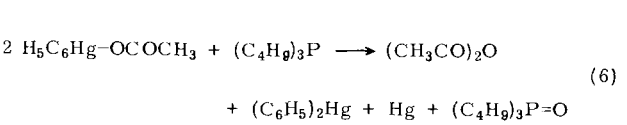
During the course of our studies on the deoxygenation of ethylene carbonate with phosphanes, it was discovered that mercury(II) acetate, which is employed as catalyst, reacts with phosphorus(III) compounds to yield acetic anhydride. We therefore turned our attention to the possible generation of active acyl groups by the coupled utilization of oxidation and reduction processes. New and practically useful reactions were found which are suitable for the preparation of acid anhydrides, esters, peptides, and nucleotides.

It was found that mercury(II) or mercury(I) salts of carboxylic acids behave as oxidizing reagents toward triethylphosphite or tri-*n*-butylphosphane, yielding the corresponding acid anhydrides along with triethylphosphate or tri-*n*-butylphosphane oxide [Eq. (5)][5], and mercury.



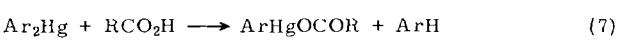
(5)

Phenylmercury(II) acetate behaves similarly toward tri-*n*-butylphosphane and affords acetic anhydride in 40—45% yield along with diphenylmercury and mercury [Eq. (6)].

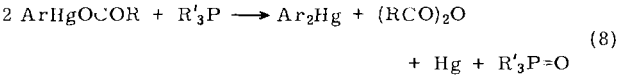


(6)

On the other hand, it is reasonable to assume that arylmercury(II) carboxylates are readily formed on reaction of diarylmercury with carboxylic acids. Hence, by combination of these two reactions it should be possible to prepare acid anhydrides from acids in accordance with equations (7) and (8).

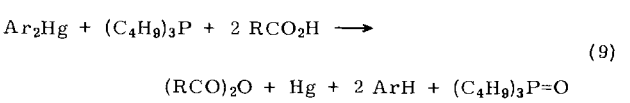


(7)



(8)

Indeed, treatment of diphenyl- or bis(*p*-methoxyphenyl)mercury with tri-*n*-butylphosphane in the presence of 2 equivalents of carboxylic acid leads to formation of the corresponding acid anhydride in high yield along with mercury and tri-*n*-butylphosphane oxide [Eq. (9)][6].



(9)

Ar = C_6H_5, *p*-CH_3O-C_6H_4

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The University of Tokyo
Bunkyo-ku, Tokyo 113 (Japan)

In this reaction, two molecules of carboxylic acid undergo condensation with the help of a hydrogen acceptor (diarylmercury) and an oxygen acceptor (tri-*n*-butylphosphane) to give the anhydride.

Since these dehydration reactions essentially proceed *via* an oxidation and a reduction process it is important that suitable oxidation reagents and reducing reagents (phosphorus(III) compounds) be chosen. It was found that similar dehydration condensation reactions take place successfully *e.g.* with trialkylphosphane and conjugated dicarbonyl compounds such as dibenzoylethylene [Eq. (10)][7].

$$H_5C_6CO{-}CH{=}CH{-}COC_6H_5 + (C_4H_9)_3P + 2\ RCO_2H \longrightarrow (RCO)_2O + H_5C_6CO{-}CH_2{-}CH_2{-}COC_6H_5 + (C_4H_9)_3P{=}O \quad (10)$$

The reaction could be further extended to phosphoric monoesters. Thus, for example, symmetrical diphenyl diphosphate[7] was produced in good yield on treating triethylammonium phenyl hydrogen phosphate with the coupling reagents [Eq. (11)].

$$H_5C_6CO{-}CH{=}CH{-}COC_6H_5 + (C_4H_9)_3P + 2\ H_5C_6O{-}P(=O)(O^{\ominus})\,M^{\oplus} \longrightarrow H_5C_6CO{-}CH_2{-}CH_2{-}COC_6H_5 + (C_4H_9)_3P{=}O + \underset{M = (C_2H_5)_3NH}{} \quad (11)$$

$$+\ H_5C_6O{-}P(=O)(O^{\ominus}){-}O{-}P(=O)(O^{\ominus}){-}OC_6H_5\ \ 2\ M^{\oplus}$$

N,*N*′-Dibenzoyl-*p*-benzoquinone diimine is found to be a more effective hydrogen acceptor. Reaction of carboxylic acids with the quinone imine and triphenylphosphane leads, in accordance with Eq. (12), to the formation of the carboxylic acid anhydride in high yield along with triphenylphosphane oxide and *p*-phenylenedibenzamide[8].

$$H_5C_6CO{-}N{=}\langle\rangle{=}N{-}COC_6H_5 + 2\ RCO_2H + (C_6H_5)_3P \longrightarrow (RCO)_2O + H_5C_6CO{-}NH{-}\langle\rangle{-}NH{-}COC_6H_5 + (C_6H_5)_3P{=}O \quad (12)$$

The phosphonium salts *(1)*, can be prepared from sulfenyl chlorides and triphenylphosphane. On treatment with sodium or triethylammonium salts of carboxylic acids they give the corresponding *S*-arylthiocarboxylates in high yield. The formation of the esters can be explained in terms of initial formation of acyloxyphosphonium thiolates *(2)* which subsequently decompose into the esters in accordance with Eq. (13)[9]. In this reaction, the sulfenyl chloride serves as oxidizing agent.

$$p\text{-}Cl{-}C_6H_4{-}S{-}Cl + (C_6H_5)_3P \longrightarrow \underset{(1)}{[(C_6H_5)_3\overset{\oplus}{P}{-}S{-}C_6H_4{-}Cl]\ Cl^{\ominus}} \xrightarrow{RCO_2^{\ominus}} [(C_6H_5)_3\overset{\oplus}{P}{-}S{-}C_6H_4{-}Cl]\ {}^{\ominus}O_2CR \longrightarrow \underset{(2)}{[(C_6H_5)_3\overset{\oplus}{P}{-}O{-}C(=O){-}R]\ {}^{\ominus}S{-}C_6H_4{-}Cl} \longrightarrow R{-}C(=O){-}S{-}C_6H_4{-}Cl + (C_6H_5)_3P{=}O \quad (13)$$

Similar results are also observed in the reaction of disulfanes with tertiary phosphane in the presence of carboxylic acids

$$R^1COOH + R^2S{-}SR^2 + R^3_3P \longrightarrow R^1CO{-}SR^2 + R^2SH + R^3_3P{=}O \quad (14)$$

which leads to the *S*-alkyl- or *S*-arylthiocarboxylates in high yields along with thiols and phosphane oxides [Eq. (14)][10].

2. Peptide Synthesis

The oxidation-reduction condensation in accordance with Eq. (13) can be extended to the preparation of carboxamides by treating sulfenamides with carboxylic acids in the presence of triphenylphosphane[11]. The key step in Eq. (15) is the formation of an acyloxyphosphonium thiolate *(3)* resulting from an exchange reaction of the sulfenyl group with a carboxylate ion.

Unfortunately, this reaction is not ideally suitable for the preparation of carboxamides because the thiol liberated in the first step reacts further with the sulfenamide to give undesirable side-products, disulfanes and amines. However, this side

$$(C_6H_5)_3P + R^3S{-}NHR^2 \longrightarrow [(C_6H_5)_3\overset{\oplus}{P}{-}SR^3]\ {}^{\ominus}NHR^2 \xrightarrow{R^1CO_2H} [(C_6H_5)_3\overset{\oplus}{P}{-}SR^3]\ {}^{\ominus}O_2CR^1 + H_2NR^2 \longrightarrow \underset{(3)}{[(C_6H_5)_3\overset{\oplus}{P}{-}O{-}C(=O){-}R^1]\ {}^{\ominus}SR^3} + H_2NR^2 \longrightarrow R^1{-}C(=O){-}NHR^2 + (C_6H_5)_3P{=}O + R^3SH \quad (15)$$

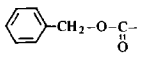
reaction can be almost completely avoided if the carboxylic acids are used in the form of their copper(II) salts; the thiolate ions are then trapped as copper(II) thiolates [Eq. (16)][12].

In this way, for example, *N*-butylhexanamide can be prepared in 95% yield from copper(II) hexanoate, triphenylphosphane, and *N*-butylbenzenesulfenamide (molar ratio 1:2:2) at room temperature. Sometimes, an excess of triphenylphosphane must be used in order to complete reaction because it is partly consumed by coordination to the copper(II) thiolate. Thus, 4 equivalents of triphenylphosphane are necessary for the reaction of *N*-benzyl-*o*-nitrobenzenesulfenamide and copper(II) benzoate[12].

$$(R^1CO_2)_2Cu + 2\ R^4S{-}NR^2R^3 + 2\ (C_6H_5)_3P \longrightarrow 2\ R^1{-}C(=O){-}NR^2R^3 + 2\ (C_6H_5)_3P{=}O + (R^4S)_2Cu \quad (16)$$

Sulfenamide derivatives of amino acids are readily available from the reaction of amino acids with sulfenyl chlorides; the sulfenyl groups are generally employed as useful amino-protecting groups in peptide synthesis. For example, reaction of the copper salt (Z-L-Phe—O)$_2$Cu with the ester Nps-Gly-OEt in the presence of triphenylphosphane affords the dipeptide derivative Z-L-Phe-Gly-OEt in high yield [Eq. (17)][12].

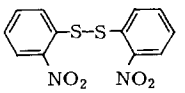
$$(Z\text{-L-Phe-O})_2Cu + 2\ Nps\text{-Gly-OEt} + 4\ (C_6H_5)_3P \quad (17)$$
$$\longrightarrow 2\ Z\text{-L-Phe-Gly-OEt} + Cu(S\text{-}C_6H_4\text{-}NO_2)_2 \cdot 2\ P(C_6H_5)_3 + 2\ (C_6H_5)_3P{=}O$$

Z =  Nps =

As shown by the Young test, a racemization takes place in this reaction, probably because of the generation of amino acid ester anions as intermediates. This, however, can be largely avoided by keeping the reaction solution neutral or weakly acidic[12]. Accordingly, free carboxylic acids can be used, as shown in Eq. (18).

$$2\ R^1CO_2H + 2\ R^3S\text{-}NHR^2 + 2\ (C_6H_5)_3P + MCl_2 + 2\ Et_3N \quad (18)$$
$$\rightarrow 2\ R^1CO\text{-}NHR^2 + 2\ (C_6H_5)_3P{=}O + (R^3S)_2M + 2\ Et_3NHCl$$

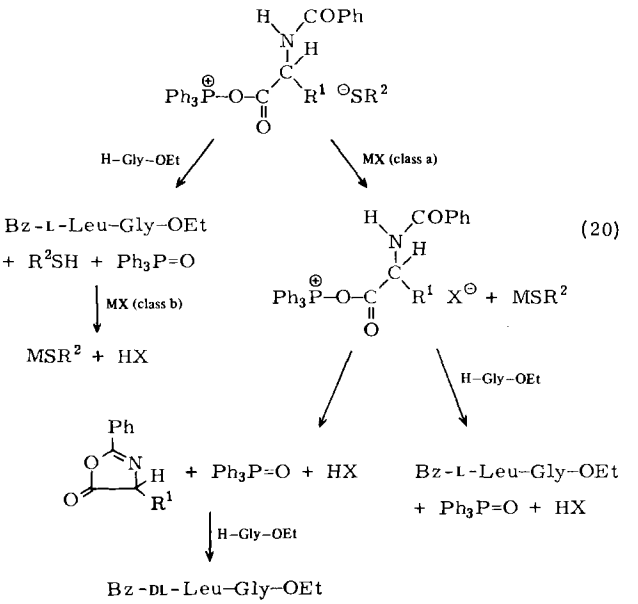
The concept of preparing acyloxyphosphonium salts from arylthiophosphonium salts can be further extended to the synthesis of peptides from triphenylphosphane, diarylsulfanes, amino acids with protected amino groups, and amino acid esters. Thus, Z-L-Phe-Gly-OEt is obtained in accordance with Eq. (19) in high yield by treating Z-L-Phe-OH with H-Gly-OEt in the presence of bis(*o*-nitrophenyl)disulfane, mercury(II) chloride, triphenylphosphane, and triethylamine.

$$Z\text{-L-Phe-OH} + H\text{-Gly-OEt} + HgCl_2 + \text{  } + Ph_3P + 2\ Et_3N \quad (19)$$
$$\longrightarrow Z\text{-L-Phe-Gly-OEt} + Hg(S\text{-}C_6H_4\text{-}NO_2)_2 + Ph_3P{=}O + 2\ Et_3NHCl$$

Other metal salts can also be employed in this reaction, but soft acids such as mercury(II), silver(I), and copper(II) salts are usually found to yield better results. This method makes it possible to synthesize peptides from *N*-protected amino acids and amino acid esters, but racemization takes place if amines are used to trap the hydrogen chloride that is formed. Attempts were therefore made to replace the bases by metal compounds which can form thiolates. These metal compounds (MX) can be classified into two categories:

a) Mercuric salts of urea, succinimide, *p*-nitrophenol *etc.* which afford thiolates on treatment with triphenylphosphane and disulfanes—probably through direct attack by the thiolate ion on the phosphonium salts. In this case, the stabilities of the X^- anions in the salts are expected to have a great effect on racemization. In accord with this assumption, the optical purity of the dipeptides is found, except in the case of *N*-hydroxysuccinimide, to increase as the X^- anion stability increases.

b) Bis(*p*-methoxyphenyl)mercury and *p*-methoxyphenylmercury(II) bromide can react only with thiols to yield mercury(II) thiolates and anisole, but cannot react with the phosphonium thiolates. With these compounds, satisfactory results can be obtained as regards yield and content of L-isomer. The high optical purity in these cases may be attributed to the fact that no oxazolone is formed. The intermediary acyloxyphosphonium salts are attacked only by H-Gly-OEt, whereupon the peptides and thiols are formed, which on reaction with mercury(II) compounds yield mercury(II) thiolates and anisole. Since anisole is produced directly through protonation of the mercury(II) compounds by thiols, no anisyl anion is present during thiolate formation and the formation of oxazolone is prevented [Eq. (20)].



(20)

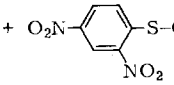
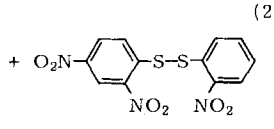
Bz = C_6H_5CO– R^1 = $-CH_2-CH(CH_3)_2$

A wide variety of solvents, excepting *N*,*N*-dimethylformamide and acetonitrile, can be used in this reaction. The yields and optical purities of the products so obtained are satisfactory[13].

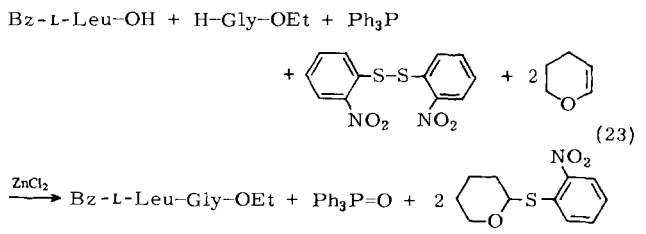
In addition to *p*-methoxyphenylmercury(II) compounds, other kinds of reagents which are reactive enough to capture thiols have also been shown to participate in this type of reaction. For example, sulfenic acid esters, which are known to react with thiols to yield disulfanes, can be effectively used as scavengers [Eq. (21)].

$$R^1S\text{-}OR^2 + R^3SH \longrightarrow R^1S\text{-}S\text{-}R^3 + R^2OH \quad (21)$$

Reaction of Bz-L-Leu-OH with Nps-Gly-OEt in the presence of triphenylphosphane and methyl 2,4-dinitrobenzenesulfenate gives [according to Eq. (22)] Bz-L-Leu-Gly-OEt in high yield and with high optical purity[14].

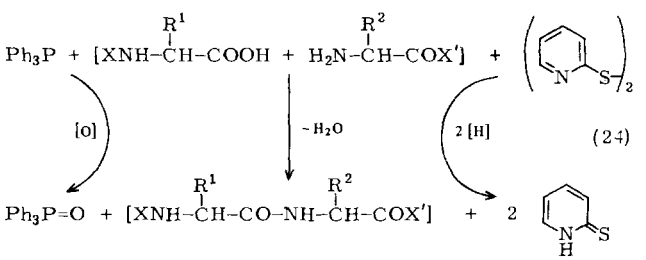
$$Bz\text{-L-Leu-OH} + Nps\text{-Gly-OEt} + Ph_3P + \text{  } \rightarrow \quad (22)$$
$$Bz\text{-L-Leu-Gly-OEt} + Ph_3P{=}O + \text{  } + CH_3OH$$

Further, in a similar reaction, vinyl ethers can also act as thiol scavengers [Eq. (23)][14].



The dipeptides obtained in both of these reactions undergo little racemization and highly optically active products are usually obtained.

Thiols such as 1-pyridinethiol, which bear the mercapto group at the α- or γ-position are well known to exist predominantly in the thione form in solution[15]. Accordingly, peptide synthesis by means of the phosphane-disulfane system appears to take place successfully in the absence of thiol scavengers when disulfanes derived from such thiols are used. In this reaction, 2-pyridinethiol—a hydrogenated product produced along with the peptides—would isomerize to the stable thione form which is unreactive towards the other reaction partners. Thus, treatment of Bz-L-Leu-OH with H-Gly-OEt in the presence of triphenylphosphane and di(2-pyridyl)disulfane is shown to lead to the formation of Bz-L-Leu-Gly-OEt in high yield [cf. Eq. (24)][14].



According to the Young test, racemization is highly suppressed in this reaction system and dipeptides with high optical purity are obtained. For example, synthetic Bz-L-Leu-Gly-OEt was shown to be 96% pure L isomer by the Young test. Other disulfanes such as bis(5-nitro-2-pyridyl)-, di(2-benzothiazolyl)- and di(2-benzimidazolyl)disulfane, which take up hydrogen and similarly isomerize to thiones are suitable for peptide synthesis, but not di(4-pyridyl)disulfane[16].

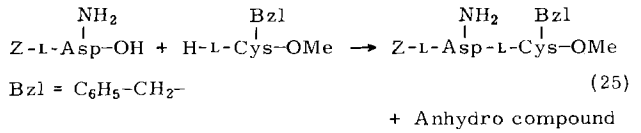
This reaction is found to offer significant advantages in peptide synthesis. It can be carried out in a wide variety of solvent systems; some modifications are necessary though when acetonitrile or *N*,*N*-dimethylformamide is used. Racemization is largely suppressed if 1 equivalent of 2(1*H*)-pyridinethione is added at room temperature to the acetonitrile (yield: 89%; L isomer: 94%) or 2 equivalents of 2(1*H*)-pyridinethione are added at −30°C to the *N*,*N*-dimethylformamide (yield: 88%; L isomer: 94%) at the beginning of the reaction. In the presence of chloride ions (use of glycine ester hydrochloride and 1 equivalent of triethylamine in chloroform), addition of 2 equivalents of 2(1*H*)-pyridinethione or *N*-hydroxysuccinimide at room temperature gives favorable results [2(1*H*)-pyridinethione (yield: 88%; L isomer: 87%); *N*-hydroxysuccinimide (yield: 91%; L isomer: 86%)].

The presence of water has little effect on the reaction. On initially adding 1 equivalent of 2(1*H*)-pyridinethione in the precence of a tenfold excess of water in dioxane the yield was 90% (L isomer, by the Young test: 94%). Further, the reaction can be carried out over a wide range of temperatures (from −70°C to the boiling point of methylene chloride). The fact that the solvent can be freely chosen makes it possible to employ the solid phase method. A specially practical merit of this method is in its compatibility with most of the other functional groups: no difficulties are encountered when methionine, cysteine, or tryptophan carbonyl groups are coupled with amino groups, and the hydroxyl groups in tyrosine, threonine and serine can be used without protection. Favorable results are also obtained in the case of nitroarginine, which is transformed into the lactam in the usual methods[17] and in the cases of glutamine and asparagine no nitrile formation is observed. For example, whereas water is frequently cleaved at the wrong position in the peptide synthesis with dicyclohexylcarbodiimide (DCC)—as in the formation of anhydro derivatives of asparagine or glutamine—the present method proceeds without complications in this connection because the triphenylphosphane/dipyridyldisulfane reagent is inert toward substrates of low acidity such as amide linkage[18]. Thus, in the reaction according to Eq. (25) with DCC as condensing agent, 35% peptide and 28% anhydro compound are formed

Table 1. Peptides synthesized by oxidation-reduction condensation.

Peptide [a]	Solvent	Yield [%]	M.p. [°C]	$[\alpha]_D$ [°]	*c*	Solvent
Z-Cys(Bzl)-Gly-OEt	CH_2Cl_2	91	97—9	−27.0	6	AcOH
Z-Trp-Gly-OEt	CH_2Cl_2	92	118—20	−19.8	2	EtOH
Z-Trp-Ile-OMe	CH_2Cl_2	93	69—70	−14.1	2.6	DMF
Z-Thr-Gly-OEt	CH_2Cl_2	83	105—7	−13.8	1	EtOH
Z-Ser-Gly-OEt	CH_2Cl_2	84	98—100	− 5.5	1	EtOH
Z-Gln-Gly-OEt	CH_2Cl_2	86	168—70	− 7.3	1	DMF
Z-Asn-Gly-OEt	DMF-CH_2Cl_2	85	185—7	− 5.6	1	DMF
Z-Arg(NO_2)-Gly-OEt	DMF-CH_2Cl_2		119—21	−15.4	2	MeOH
Z-Cys(Bzl)-Pro-Leu-Gly-NH_2	DMF	86	169—70	−59.4	2.5	DMF
Z-Cys(Bzl)-Tyr-Ile-Gln-Asn-Cys(Bzl)-Pro-Leu-Gly-NH_2	DMF	91	242.4 (dec.)	−44.1	2	DMF
Z-Ala-Gly-Leu-$(Gly)_3$-Leu-Gly-NHNHBOc	DMF	70	213.5			

[a] All optically active amino acids were of the L-configuration.



Bzl = C_6H_5-CH_2- (25)

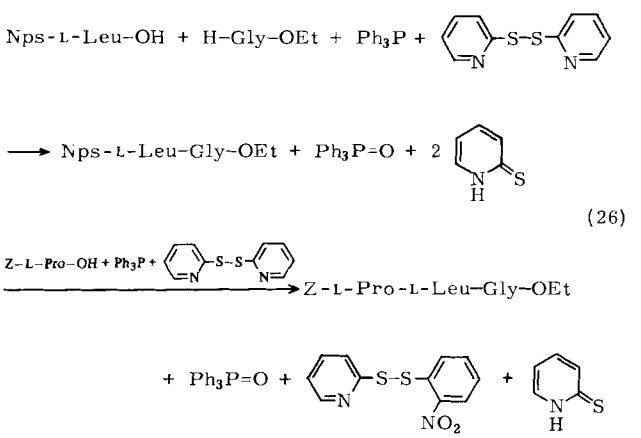
+ Anhydro compound

whereas by oxidation-reduction condensation 73% peptide and only a trace of anhydro compound are obtained.

Hence, analytically pure peptides can be prepared by this extremely simple procedure. Peptides with functional groups in the side chains that have so far been obtained by this procedure are listed in Table 1.

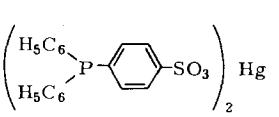
The triphenylphosphane/dipyridyldisulfane reagent (abbrev. $Ph_3P/(PyS)_2$) is very useful for the elongation of a peptide chain by two amino residues. For example, coupling of Nps-L-Leu-OH and H-Gly-OEt by $Ph_3P/(PyS)_2$, followed by the usual washing and drying, and subsequent treatment of the reaction mixture containing Nps-L-Leu-Gly-OEt with Z-L-Pro-OH and $Ph_3P/(PyS)_2$ afforded Z-L-Pro-L-Leu-Gly-OEt in 78% yield [Eq. (26)]. Z-L-Ile-L-Gln-L-Asn-OBu^t was likewise obtained in 72% yield by coupling Z-L-Ile-OH with Nps-L-Gln-L-Asn-OBu^t. Formation of pyroglutamine was not observed; hence, this method is suitable for the synthesis of glutamyl peptides.

Acylamino acids with free COOH groups can also be prepared by oxidation-reduction condensation[18]. The active pentachlorophenyl esters of Gln, Asn and Arg(NO_2) precipitate from the reaction mixture as crystalline products and



(26)

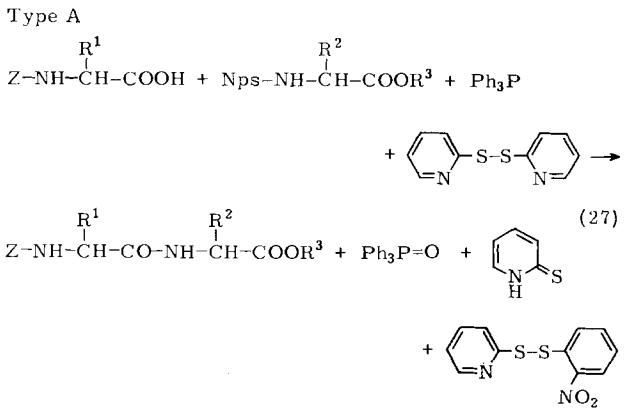
are already analytically pure after simple filtration and washing. More soluble active esters were prepared using the modified phosphane, mercury bis(diphenylphosphinobenzenesulfonate). The phosphane oxides that are formed are removed by washing with water, and the active esters are purified by one recrystallization.



The peptide syntheses by oxidation-reduction condensation with $Ph_3P/(PyS)_2$ are summarized in Equations (27)—(29).

Biologically active oxytocin can be conveniently prepared with these reactions. The protected nonapeptide was obtained in 91% yield by a type C reaction using 50% excess of reagents. After HF treatment and air oxidation, the synthetic oxytocin (in solution) showed a depressor activity of 104 unit/mg[19].

Type A



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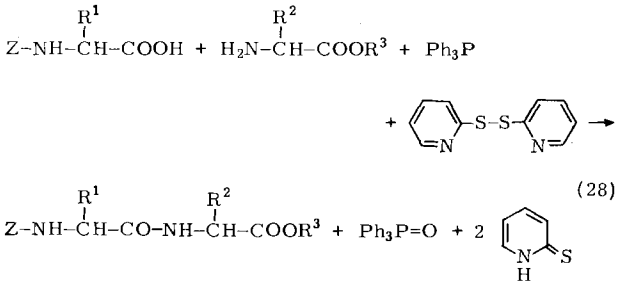
Type B



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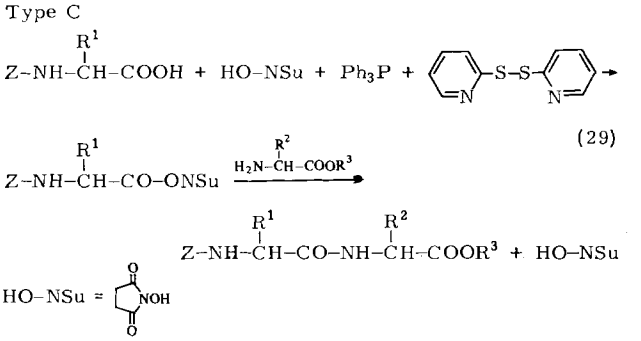
Type C



(29)

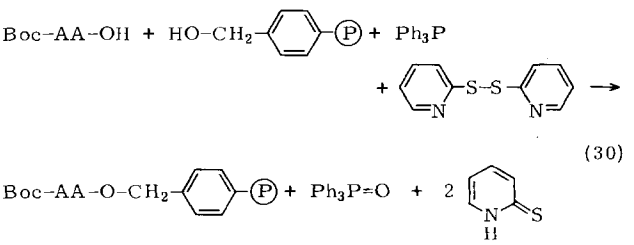
Application of the oxidation-reduction condensation method to solid phase peptide synthesis was also investigated. This study was focused on developing a general procedure for anchoring the first C-terminal amino acid to the polymer support.

In the solid phase peptide synthesis with DCC, the peptide linkages are formed under mild conditions. However, introduction of the first amino acid into the resin necessitates refluxing the amino acids and the resin at 80°C for 48 h. It seems desirable that both the attachment of the first amino acid to the resin and the subsequent couplings can be carried out under mild conditions using the same procedure. Hence the utilization of oxidation-reduction condensation for this purpose was investigated. First, the usual 2% crosslinked chloromethyl resin (Schwarz-Mann, New York, Cl content 2.0 mmol/g) was converted by a well known procedure into a hydroxymethyl resin. Esterification of this resin with various amino acids and peptide fragments [Eq. (30)] was studied; some favorable results were obtained.

Amino acids and peptide fragments are easily attached to the resin by this procedure. No nitrile formation or transesterification was observed in the case of Asp and Glu. Favorable results were also obtained with Arg, Cys and Trp whose

attachment to the resin has previously never been reported. Boc-Met-OH and Boc-His(Bzl)-OH can also be attached.

This method has the following special merits in solid phase peptide synthesis: All Boc amino acids and peptides tested so far can be attached in any desired amount and in relatively homogeneous environment on the resin. This esterification



(30)

AA = Amino acid residue Ⓟ = Polymer;
Boc = $(CH_3)_3C$–O–CO–

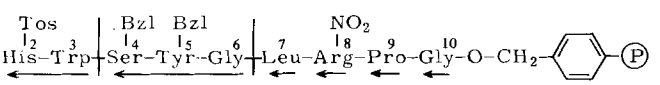
proceeds more rapidly and under milder conditions than in the ordinary method. Moreover, the reaction conditions and preparative operations are the same as for subsequent chain-lengthening acylations and, consequently, incorporation of the esterification step in the automated process is possible. Utilization of this method has led to the successful synthesis of bioactive LH-RH and ACTH.

2.1. Synthesis of LH-RH

LH-RH is the hormone which liberates the luteinizing hormone. Pure LH-RH with the full activity of natural LH-RH was synthesized by oxidation-reduction condensation of peptide fragments on a solid support by employing two types of chain elongation, that from C-terminal amino acid (type A elongation) and that from N-terminal amino acid (type B elongation)[20].

2.1.1. Type A Chain Elongation

The synthesis of the LH-RH-nonapeptide (2—10 sequence) was successfully achieved by the solid phase method as shown in (31). Each arrow corresponds to a coupling step.

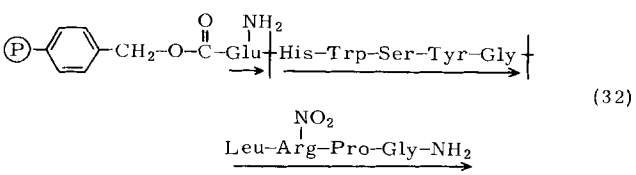


(31)

The nonapeptide was liberated by ammonolysis and was converted into LH-RH by coupling with Glu-OPcp (Pcp = pentachlorophenyl).

2.1.2. Type B Chain Elongation

The building of decapeptide was achieved by employing the three fragments with the 1, 2—6 and 7—10 amino acid sequences as shown in (32).



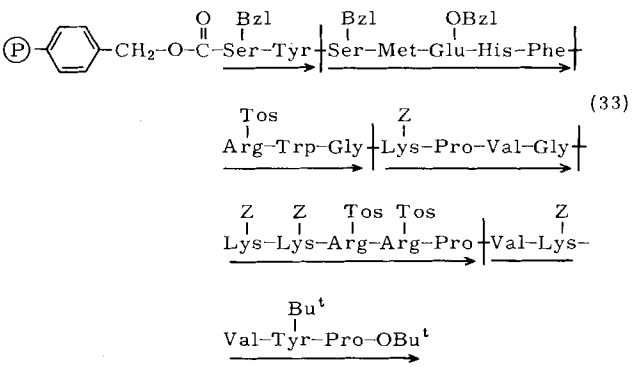
(32)

The decapeptide amide is liberated from the resin with HF and converted into LH-RH by cyclization of the glutaminyl residue. Fully active LH-RH is obtained in 51% yield based on glutamine-resin employed.

In this way, chain elongation can be carried out with minimum protection of side chains and excess amino components can be recovered unchanged.

2.2. Synthesis of $ACTH^{1-24}$

$ACTH^{1-24}$ is synthesized on a solid support by oxidation-reduction condensation as shown in (33)[21].



(33)

The synthesis begins with the N-terminal amino acid (type B elongation). The coupling rates were monitored during the reaction by quantitative determination of the fragments in solution by high pressure liquid chromatography on aminated Hitachi Gel 3010[22].

Pure $ACTH^{1-24} \cdot 7\,AcOH \cdot 9\,H_2O$ was obtained in 25% yield from the initial resin-Ser-Tyr after HF treatment and purification on Sephadex G-25 and carboxymethylcellulose. Amino acid ratios determined after complete enzymatic digestion and acid hydrolysis were in good agreement.

The ACTH activity of this purified peptide was assayed by the ascorbic acid depletion test according to U.S.P. XVIII. Referred to the 2nd international standard it exhibited an activity of 96 (83—128) IU/mg. This value agrees with that given in the literature.

Some of the particular merits of this method for the peptide synthesis are as follows: i) unreacted amino acid derivatives can be recovered and accordingly can be recycled in the chain elongation procedure; ii) the number of protecting groups on the side chains can be reduced; iii) smaller peptide fragments can be synthesized by classical methods from readily available Z-amino acids; iv) diacylations are avoided since excess amino acid derivatives are used in solution; v) the end product is homogeneous since contaminations by similar peptides are eliminated; vi) the number of acidolyses can be reduced—which is of importance for the acid-sensitive tryptophan residue; vii) the progress and completeness of each coupling reaction is easily monitored by high pressure liquid chromatography.

The versatility of this approach, along with a combination of classical syntheses in solution, opens up new possibilities for facile preparation of pure long-chain peptides and significantly extends the scope of solid phase peptide synthesis.

3. Nucleotide Synthesis

The oxidation-reduction condensation reaction can also be used for the synthesis of nucleotide derivatives.

3.1. Synthesis of Nucleoside 2',3'- and 3',5'-Cyclophosphates

Nucleoside-2',3'- and -3',5'-cyclophosphates can be synthesized by oxidation-reduction condensation from nucleoside-2'- and -5'-phosphates, respectively[23]. Table 2 lists some compounds which have so far been obtained in this way.

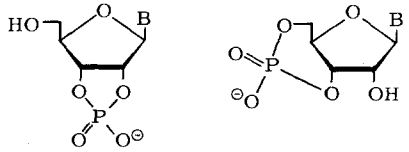


Table 2. Nucleoside cyclophosphates synthesized by oxidation-reduction condensation.

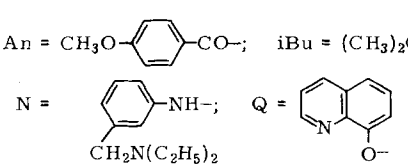
Nucleotide	Yield [%]	Nucleotide	Yield [%]
2',3'-cyclic AMP	quant.	3',5'-cyclic AMP	85
2',3'-cyclic CMP	quant.	3',5'-cyclic CMP	56
2',3'-cyclic GMP	quant.	3',5'-cyclic GMP	85
2',3'-cyclic UMP	quant.	3',5'-cyclic UMP	80
4',5'-cyclic FMN [a]	quant.	3',5'-cyclic TMP	70

[a] FMN refers to flavin mononucleotide.

3.2. Synthesis of Oligonucleotides

3'—5'-linked deoxyribooligonucleotides such as dinucleoside phosphates[23], dinucleotides[24], trinucleoside diphosphates[23, 25], and trinucleotides[26] can also be synthesized in high yields by the new method. A selection of these is shown in Table 3.

Table 3. Oligonucleotides synthesized by oxidation-reduction condensation.

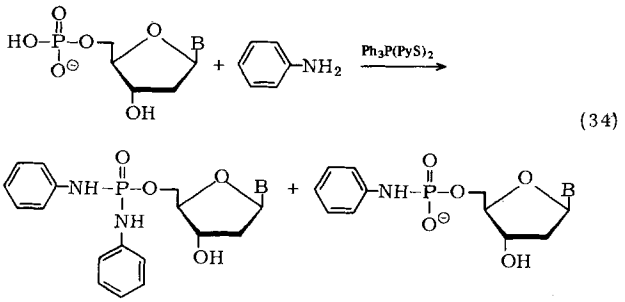


Nucleotide	Yield [%]	Nucleotide	Yield [%]
d(TpT)	90	d(TpC)	84
d(TpA)	86	d(TpG)	80
d(NpA^{Bz}pA^{Bz}OAc)	51	d(NpTpTOAc)	50
d(QpTpC^{An}OAc)	58	d(QpTpG^{iBu}OAc)	55
d(TpApT)	60	d(ApApA)	60
d(NpA^{Bz}pTpTOAc)	74	d(NpA^{Bz}pTpG^{iBu}OAc)	21

Further, TpTpTpT was obtained in 50% yield from TpTpT and 3 equivalents of 3'-*O*-acetylthymidine 5'-phosphate.

3.3. Synthesis of Oligonucleotides with Phosphorodianilidates

Nucleotide 5'-phosphorodianilidates were prepared as shown in the following scheme [Eq. (34)]. The results are summarized in Table 4[27].



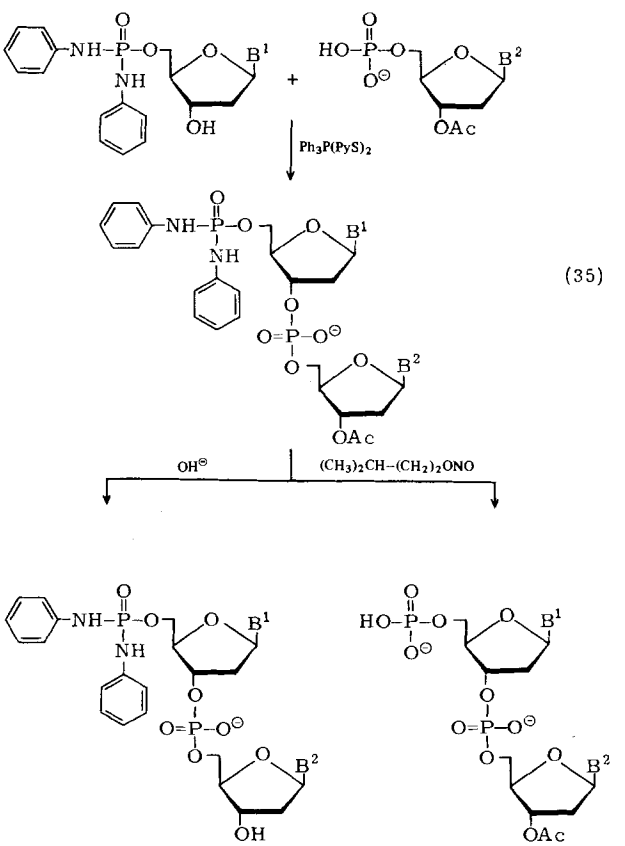
(34)

Table 4. Nucleotide 5'-phosphorodiamidate synthesized by oxidation-reduction condensation.

B	Amine	Reaction time (days)	Yields [%] Phosphoro-monoamidate	Phosphoro-diamidate
T	aniline	2	35	65
T	morpholine	5 [a]	82.5	17.5
		1	57	43
		3	17	64
A^{Bz}	aniline	2	35	65
C^{An}	aniline	2	41	59
G^{iBu}	aniline	2	40	60

[a] Five hours.

Protected dinucleotides (cf. Table 5)[27] can be obtained by condensation of the phosphorodianilidates with protected mononucleotides according to Eq. (35).

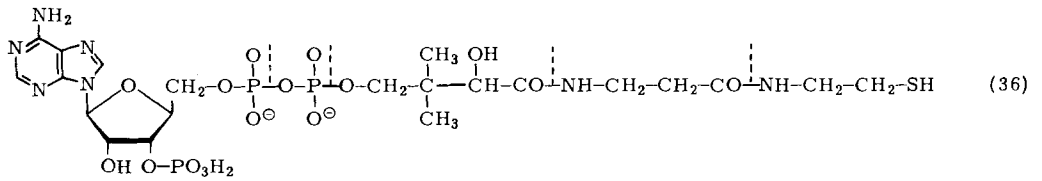


(35)

Table 5. Protected dinucleotides with 5'-phosphate groups synthesized by oxidation-reduction condensation.

Dinucleotide	B^1	B^2	Amount [mmol]	$Ph_3P/(PyS)_2$ [mmol]	Yield [%]
d(pTpTOAc)	dpT	dpTOAc	0.1	0.5	70
d(pTpC^{An}OAc)	dpT	dpC^{An}OAc	0.07	0.5	50
d(pTpA^{Bz}OAc)	dpT	dpA^{Bz}OAc	0.07	0.5	51
d(pA^{Bz}pTOAc)	dpA^{Bz}	dpTOAc	0.1	1	75
d(pA^{Bz}pA^{Bz}OAc)	dpA^{Bz}	dpA^{Bz}OAc	0.1	1	70
d(pA^{Bz}pC^{An}OAc)	dpA^{Bz}	dpC^{An}OAc	0.1	1	70

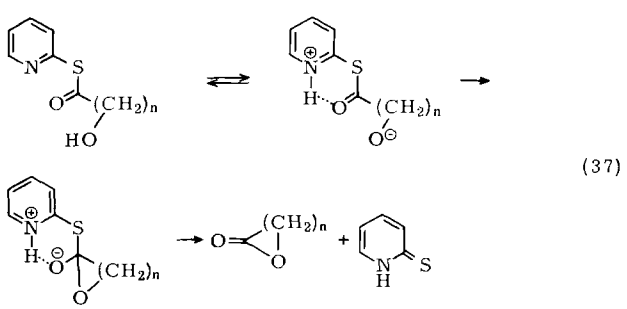
The total synthesis of coenzyme A by utilization of oxidation-reduction condensation in each important step was accomplished in accordance with (36)[28].



(36)

4. Macrolide Synthesis

The oxidation-reduction condensation was used by *Corey et al.*[29] for the internal esterification of hydroxy acids whereby medium- and large-ring lactones are formed. The method proved highly effective and yet mild enough to be used with complex and polyfunctional substrates. *Corey et al.* developed this reaction on the basis of the following consideration: One way of simultaneously activating both the carboxyl and hydroxyl groups for mutual reaction would be to utilize a carboxylic derivative which would favor proton transfer from hydroxyl to carboxylic oxygen. By way of example, an *S*-2-pyridyl ester of an ω-hydroxymonothiocarboxylic acid reacts as shown in Eq. (37). As indicated in Table 6, good to excellent yields are obtained except in the case of the nine-membered ring.



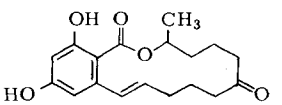
(37)

Table 6. Synthesis of lactones and dimeric lactones (diolides) by cyclization of the *S*-2-pyridyl esters of ω-hydroxycarboxylic acids ($n = 5, 7, 10, 11, 12, 14$) in xylene. After slow addition of thioate to refluxing xylene the whole was further refluxed for a further 10 h.

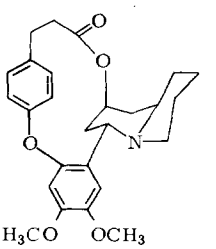
	Lactone			Diolide	
n	Ring size	GLC yield [%]	Isolated yield [%]	Ring size	Isolated yield [%]
5 [a]	7	87	71	14	7
7 [b]	9	25	8	18	41
10 [c]	12	64	47	24	30
11	13	76	66	26	7
12	14	79	68	28	6
14	16	88	80	32	5

[a] Solvent benzene; [b] reaction time 30 h; [c] reaction time 20 h.

The method can also be used for the lactonization of more complex hydroxy acids. Thus a series of novel macrocyclic lactones, such as (±)-zearalenone, prostaglandin F_2 1,9-lactone, prostaglandin F_2 1,15-lactone, the lactone of the polyether antibiotic monensin, brefeldin A, carpaine, vertaline, and erythronolide B were obtained from the hydroxy acid derivatives[29–31].



(±)-Zearalenone

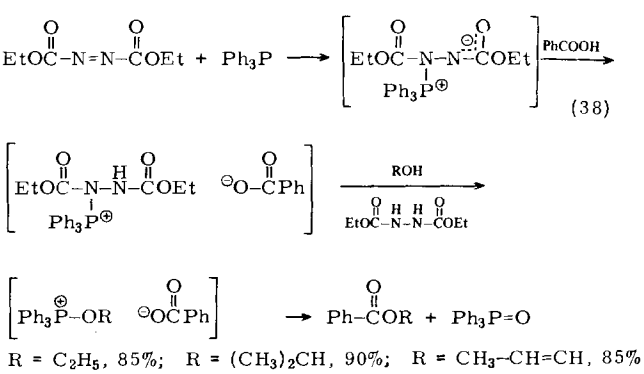


Vertaline

5. Related Reactions

5.1. Oxidation-Reduction Condensations with Triphenylphosphane and Diethylazodicarboxylate

Intermolecular and intramolecular dehydrations with triphenylphosphane and diethylazodicarboxylate have been reported by *Mitsunobu et al.*[32]. The reaction of benzoic acid with alcohols in the presence of this reagent at room temperature resulted in the formation of the corresponding carboxylic esters in good yields. The reaction is assumed to proceed *via* an alkoxyphosphonium salt as shown in Eq. (38).

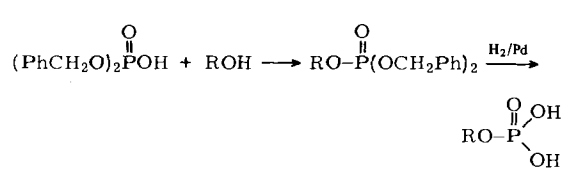


(38)

R = C_2H_5, 85%; R = $(CH_3)_2CH$, 90%; R = CH_3–CH=CH, 85%

Similarly, thymidine and uridine react with carboxylic acids to give the corresponding 5'-*O*-acylnucleosides in good yields[33].

Dibenzyl hydrogen phosphate reacts smoothly with alcohols and with nucleosides in the presence of triphenylphosphane and diethylazodicarboxylate, and after hydrogenolysis, alkyl- and nucleoside-5'-dihydrogen phosphate are formed in good yields[34, 35]. Selective phosphorylation of nucleosides can be effected by this procedure [Eq. (39)][35].



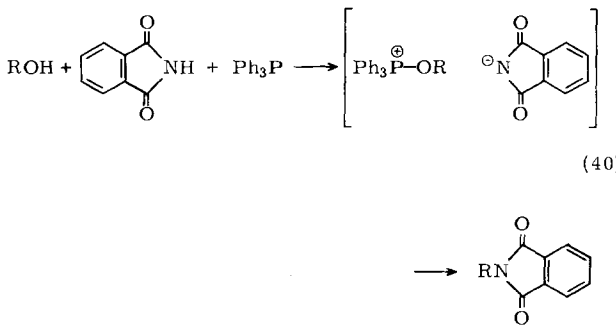
(39)

ROH = C_2H_5OH, 92%; ROH = n-C_3H_7OH, 96%;
ROH = Thymidine, 77%; ROH = Uridine, 63%

That the reaction involves initial activation of alcohol was proved by the reaction of an optically active (*S*)-(+)-2-octanol with benzoic acid to give (*R*)-(−)-2-octyl benzoate in high optical yield[34]. *Bose et al.*[36] have reported that the present system could be utilized for inversion of configuration of unhindered steroids. Treatment of steroid alcohols with carboxylic acids in this way, furnishes stereochemically pure esters with inverted configuration in good yield (75—100%).

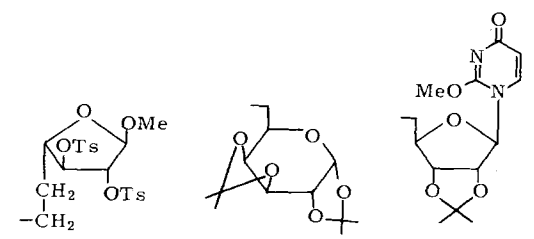
The reaction should therefore be rationalized in terms of alkylation of the carboxylic acid or phosphoric acid rather than acylation or phosphorylation of the alcohol. Namely, the alkoxyphosphonium salt is a strong alkylating reagent.

This system has been used in the alkylation of weak acids such as imides and compounds containing active methylene groups. Thus, reaction of phthalimide with alcohols gives *N*-alkylphthalimides in yields of 60—90% [Eq. (40)][37-39]. Since these products are converted into amines on treatment with hydrazine hydrate, the reaction provides a means of converting alcohols into amines.

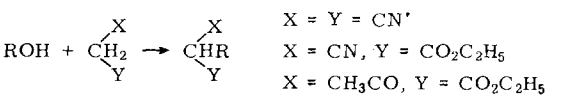


(40)

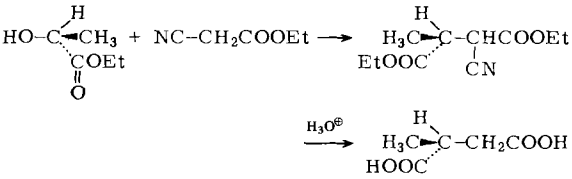
R = CH_3–CH=CH–CH_2–, C_2H_5–, CH_2=CH–CH_2–, n-C_3H_7–, $ClCH_2$–CH_2–, n-C_4H_9–, $C_2H_5O_2C$–CH_2–, CH_3–CH(C_2H_5)–, CH_3–, CH_3–CH(C_6H_{13})–, –C(H)(CH_3)(C_6H_{13})



Moreover, compounds with active methylene groups can also be alkylated with diethylazodicarboxylate and triphenylphosphane [Eq. (41)]. The yield of alkylated product increases



(41)



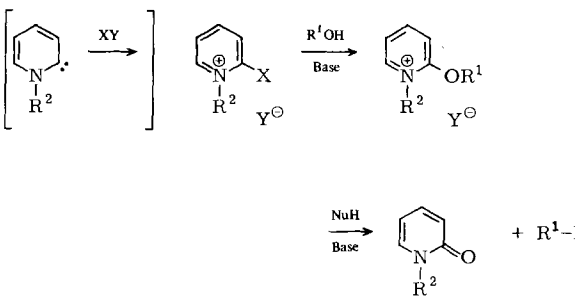
(42)

to 80% when the reaction mixture is allowed to stand for several days. Since the reaction takes place under mild neutral conditions, the procedure ought to be suitable for the synthesis of optically active compounds [Eq. (42)][40].

Recently, *Bittner* and *Assaf* reported that the present system can be utilized for the preparation of aryl ethers. The yield of ether is 75—80% within two hours, while the maximum yield (80—98%) is obtained after the reaction mixture has been left to stand for an additional 12 hours at room temperature[41].

5.2. Condensations with Pyridinium Salts

Recently, a new type of dehydration condensation reaction with pyridinium salts has been developed[42]. This reaction has a wide scope of application; it is suitable, for example, for the synthesis of esters, amides, and phosphoric esters and for alkylations.



(43)

If it is assumed that the pyridinium salt is formed from the given carbene-like species, then the overall reaction could be classed as an oxidation-reduction condensation.

Since all reaction steps take place with involvement of the pyridinium salt, the condensation reaction should be favored from the point of view of entropy. Indeed, the preparation of esters and amides proceeds in high yields even with equivalent amounts of the reactants. Consequently, it would appear that the reaction can be resorted to in numerous synthetic schemes.

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COMMUNICATIONS

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

Novel 1,2,4-Thiadiazolidine 1-Oxides and 1,1-Dioxides from 2-Imino-1,3-thiazetidines

By *Walter Ried*, *Oskar Mösinger*, and *Walter Schuckmann*[*]

The action of hydrogen peroxide/glacial acetic acid on 2-imino-1,3-thiazetidines *(1)*, which are accessible from *N,N'*-disubstituted thioureas, diiodomethane, and triethylamine[1,2], leads not to the 2-imino-1,3-thiazetidine 1,1-dioxides *(3)*, but, surprisingly, with ring expansion to the 3-oxo-1,2,4-thiadiazolidine 1-oxides *(5)*. The oxidation products were identified by X-ray structure analysis of *(5b)* and *(5c)*[3] since no distinction could be made between the isomers *(3)*—*(5)* on the basis of spectroscopic data (Table 1). The 1,2,4-thiadiazolidine 1-oxide system was recently mentioned for the first time in another connection[4].

We assume that *(5)* is formed *via* the two non-isolable intermediates *(2)* and *(4)*. The initially formed *S*-oxide *(2)* experiences an oxygen insertion resulting in ring expansion analogous to the Baeyer-Villiger oxidation to give *(4)*. Subsequent Dimroth rearrangement leads to *(5)*.

Oxidation of *(5)* with H_2O_2/glacial acetic acid furnishes the 3-oxo-1,2,4-thiadiazolidine 1,1-dioxides *(6)* (Table 1). The reaction affords a novel entry to this class of compound, whose preparation was first reported only recently[5].

1,2,4-Thiadiazolidine 1-oxides (5) and 1,1-dioxides (6)

To a solution of *(1)* (5 mmol) in glacial acetic acid (50 ml) [in the case of *(1f)* 150 ml] is added 2.1 equivalents of hydrogen peroxide (35% aqueous solution). The mixture is allowed to stand for 6 days at room temperature and the solvent removed by distillation in a rotary evaporator. The residue, in the case of *(5e)* and *(5f)*, is recrystallized (white needles) from ethanol. In the case of *(5a)*—*(5d)* the residue is taken up in chloroform, filtered, and the filtrate evaporated to dryness. *(5a)* crystallizes on addition of ethanol/*n*-hexane; *(5b)*—*(5d)* are obtainable (as white crystals) after recrystallization from ethanol.

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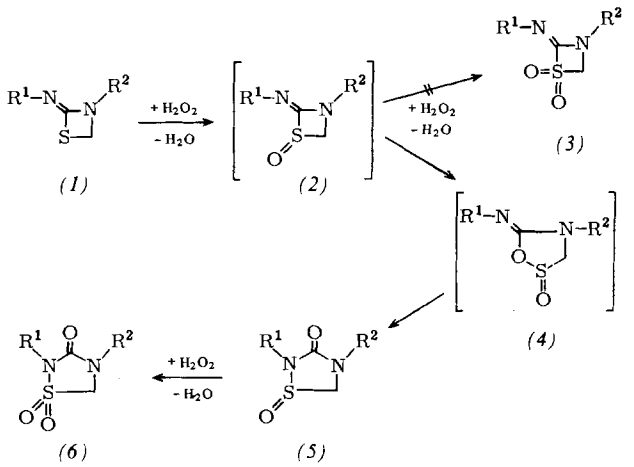

Table 1. Data for compounds *(5)* and *(6)*. Correct analyses were obtained for all compounds.

	R^1	R^2	*(5)* Yield [%]	M.p. [°C]	IR [a] [cm^{-1}]	^{1}H-NMR [b, c] [δ, ppm] q	*(6)* Yield [%]	M.p. [°C]	IR [d] [cm^{-1}]	^{1}H-NMR [b] [δ, ppm] s
(a)	$CH(CH_3)_2$	C_6H_5	72	86	1690, 1089	4.45	35	111.5	1707, 1161	4.70
(b)	CH_3	C_6H_5	34	166	1694, 1080	4.48	31	137 (dec.)	1715, 1159	4.79
(c)	$C_6H_5CH_2$	C_6H_5	53	143	1692, 1098	4.44				
(d)	o-$CH_3C_6H_4CH_2$	C_6H_5	60	107.5	1700, 1099	4.45	13	108.5	1725, 1152	4.80
(e)	C_6H_5	C_6H_5	46	140	1700, 1105	4.62	11	120.5 (dec.)	1725, 1159	4.95
(f)	C_6H_5	p-$NO_2C_6H_4$	46	168	1725, 1092	4.73	10	254 (dec.)	1740, 1148	5.00

[a] νC=O and νS=O in KBr.
[b] Methylene groups in the heterocycle relative to HDMSO as internal standard, in $CDCl_3$.
[c] $J_{AB} = 11.0$ Hz.
[d] νC=O and νSO_2 in KBr.

A solution of *(5)* (2 mmol) in glacial acetic acid (50 ml) is treated with 1.2 equivalents of hydrogen peroxide (35% aqueous solution) and allowed to stand for 4 weeks at room temperature. The solution is evaporated under vacuum, and compound *(6)* isolated from the residue by column chromatography on silica gel (eluant: benzene/ethyl acetate 4:1). Recrystallization from ethanol affords *(6)* as white crystals.

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(1a), 58151-15-8; *(1b)*, 58151-16-9; *(1c)*, 50500-04-4; *(1d)*, 58151-17-0; *(1e)*, 50500-03-3; *(1f)*, 58151-18-1; *(5a)*, 58151-04-5; *(5b)*, 58151-05-6; *(5c)*, 58151-06-7; *(5d)*, 58151-07-8; *(5e)*, 58151-08-9; *(5f)*, 58151-09-0; *(6a)*, 58151-10-3; *(6b)*, 58151-11-4; *(6d)*, 58151-12-5; *(6e)*, 58151-13-6; *(6f)*, 58151-14-7

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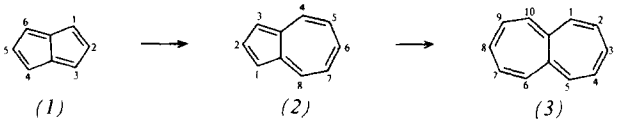
Cycloadditions of Pentalene and Azulene—A Facile Heptalene Synthesis[**]

By *Klaus Hafner, Herbert Diehl,* and *Hans Ulrich Süss*[*]

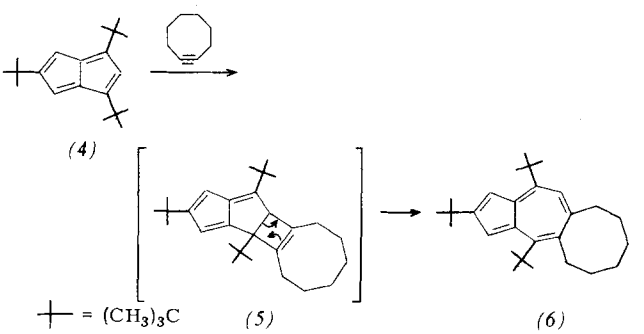
The two lowest homologs of the annulene series, *i.e.* cyclobutadiene and benzene, are known to undergo either thermally or photochemically induced [2+4] and [2+2] cycloadditions with reactive alkynes to give cyclobutene derivatives. Valence isomerization of the latter affords the next higher vinylogous annulene, *i.e.* benzene and cyclooctatetraene respectively[1,2]. A similar transformation should also be feasible



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

in the homologous series of nonalternant bicyclic hydrocarbons pentalene *(1)*, azulene *(2)*, and heptalene *(3)*, which differ from each other by possessing one additional vinylene group each, and thus provide new entries to these ring systems. Studies on transformations of cyclopent[*cd*]azulene[3], 1,3-bis(dimethylamino)pentalene[4], and hexaphenylpentalene[5] with dimethyl acetylenedicarboxylate into derivatives of aceheptylene and azulene prompted us to investigate the ring expansion of *(1)* to *(2)* and above all that of *(2)* to *(3)*. In the course of this work we discovered a surprisingly simple and universal synthesis of stable heptalene derivatives.

Conversion of *pentalene* into *azulene:* As expected, *(4)*[6] which is the simplest pentalene derivative hitherto isolated, rapidly reacts with activated alkynes and especially with the highly strained cyclooctyne at 270 °C (presumably *via* intermediate formation of the cyclobutene derivative *(5)*) to give a 70% yield of 2,4,12-tri-*tert*-butyl-5,6,7,8,9,10-hexahydrocycloocta[*f*]azulene *(6)* (blue radial needles, m.p. 70—72 °C)[7].



(4) *(5)* *(6)*

Exclusive formation of *(6)* even at high temperatures indicates on the one hand the lack of tendency of dimerization of *(4)*, in contrast to pentalene and its methyl derivatives[8] and on the other the marked effect of substituents upon product formation. As in the dimerization of 2-methylpentalene[8] and 1,5-dimethylpentalene[9], cycloaddition in the five-membered ring of *(4)* bearing an alkyl group in position 2 (≡ 5) is hindered—mostly for obvious steric reasons.

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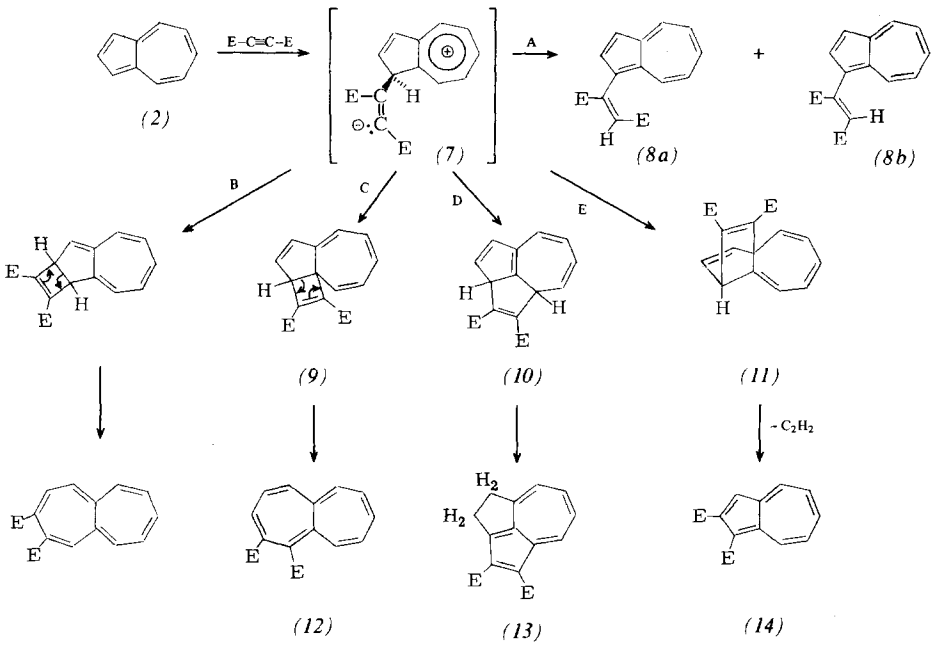
Conversion of *azulene* into *heptalene*: According to an observation by *W. Treibs*[10], azulene *(2)* reacts with acetylenedicarboxylic acid and its esters at elevated temperature and especially in the presence of Lewis acids *via* additive substitution to give 1-azulenylmaleic acid and its esters of type *(8b)*, the resonance stabilized dipolar intermediate *(7)* probably being formed first. It was expected that this intermediate can stabilize basically not only by re-aromatization of the azulene system to give *(8)* but also initially by formation



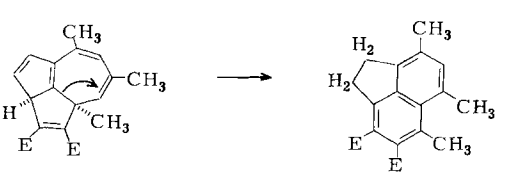
E = $COOCH_3$

of one or several cycloadducts *(9)*—*(11)*. We suspected that *(8)* is formed preferentially in the presence of proton donors or reagents promoting a proton shift, while in their absence the paths B-E may also play a role. Our experiments did confirm these expectations.

Reaction of *(2)* with dimethyl acetylenedicarboxylate in boiling tetralin in the presence of 5% trifluoroacetic acid (1 h) affords 35% of a 1:1 mixture of dimethyl 1-azulenylfumarate *(8a)* and 1-azulenylmaleate *(8b)* (olive green oil)[11] (path A). In contrast, the same reaction of *(2)* without trifluoroacetic acid added does not afford *(8)* but rather 15% of the thermally and air-stable dimethyl 1,2-heptalenedicarboxylate *(12)* [red leaflets, m. p. 114—115 °C; UV (*n*-hexane): $\lambda_{max}=204$ ($\log\varepsilon=4.36$), 266 (4.29), 337 (3.63); 60 MHz ^{1}H-NMR ([D_6]acetone): $\tau=2.73$ (d, $J=7$ Hz, H-3); 3.30—4.30 (m, 7H), 6.29 and 6.36 (s, 2$COOCH_3$)] together with 1% of dimethyl 3,4-dihydro-1,2-cyclopent[*cd*]azulenedicarboxylate *(13)* (violet crystals, m. p. 138—139 °C) and 1% of dimethyl 1,2-azulenedicarboxylate *(14)* (reddish violet crystals, m. p. 49—50 °C)[12]. *(12)*—*(14)* can easily be separated by column chromatography [Al_2O_3; *n*-hexane/ether (5:1)] on account of their different R_f values and colors.

In accord with our assumption, the heptalene derivative *(12)* should result from valence isomerization of *(9)* (path C), the tricyclic species *(13)* from rearomatization of the primary adduct *(10)* to the azulenoid system (path D), and *(14)* from a cycloreversion of the adduct *(11)* with elimination of acetylene (path E). Formation of *(14)* formally resembles the [2+8] cycloaddition of heptafulvene with dimethyl acetylenedicarboxylate, which has already been observed by *Doering et al.*[12] and leads to the same azulene derivative. The surprisingly simple formation of *(12)* from *(2)*, which is also available in larger quantities, provides a convenient preparative entry to numerous derivatives of the heptalene system. That system has hardly been studied and was hitherto only accessible in very low overall yields[13]; its stabilization by two ester groups in positions 1 and 2 corresponds to that of the 3,8-heptalenedicarboxylic ester recently described by *Vogel et al.*[13b]. The spectroscopic properties of *(12)* are in agreement with the nonplanar structure of the bicyclic system, established by X-ray structure analysis[14].

Similarly to *(2)*, alkylated azulenes react with dimethyl acetylenedicarboxylate to form corresponding alkyl derivatives of *(8)*, *(12)*, *(13)*, and *(14)*. Thus the analogous reaction of 4,6,8-trimethylazulene in the presence of 5% trifluoroacetic acid yields 25% each of dimethyl 4,6,8-trimethyl-1-azulenylfumarate (violet crystals, m. p. 106—107 °C) and -maleate (violet crystals, m. p. 109—110 °C) (path A), and 5% of dimethyl 4,6,8-trimethyl-1,2-azulenedicarboxylate (reddish violet crystals, m. p. 138—139 °C) (path E). In contrast, the same reaction in the absence of protic acids leads to 45% of a mixture of thermally stable dimethyl 6,8,10-trimethyl-2,3- and 1,2-heptalenedicarboxylate[11] in the ratio 1:2.5 (paths B and C)



besides 5% of dimethyl 4,6,8-trimethyl-1,2-azulenedicarboxylate (path E) and 4% of dimethyl 5,6,8-trimethyl-3,4-acenaphthylenedicarboxylate *(16)* (yellowish needles, m. p. 179—181 °C) arising from skeletal rearrangement and by hydrogen shift from the adduct *(15)* analogous to *(10)* (path D).

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(1), 250-25-9; *(2)*, 275-51-4; *(3)*, 257-24-9; *(4)*, 50356-52-0; *(5)*, 58150-89-3; *(6)*, 58150-90-6; *(8a)*, 58150-91-7; *(8b)*, 58150-92-8; *(9)*, 58150-93-9; *(10)*, 58150-94-0; *(11)*, 58150-95-1; *(12)*, 58150-88-2; *(13)*, 58150-96-2; *(14)*,

39479-45-3; *(15)*, 58150-97-3; *(16)*, 58150-98-4; cyclooctyne, 1781-78-8; dimethyl acetylenedicarboxylate, 762-42-5; 4,6,8-trimethylazulene, 941-81-1; dimethyl (4,6,8-trimethyl-1-azulenyl)fumarate, 58150-99-5; dimethyl (4,6,8-trimethyl-1-azulenyl)maleate, 58151-00-1; dimethyl 4,6,8-trimethyl-1,2-azulenedicarboxylate, 58151-01-2; dimethyl 6,8,10-trimethyl-2,3-heptalenedicarboxylate, 58151-02-3; dimethyl 6,8,10-trimethyl-1,2-heptalenedicarboxylate, 58151-03-4

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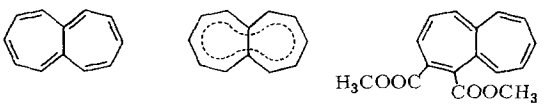

(1a) *(1b)* *(2)*

the bicyclic system from the ^{1}H-NMR spectrum of heptalene[2]. *Vogel, Oth, et al.* synthesized heptalene and stabilized heptalenes, and found heptalene to undergo a fast π-bond shift with an activation energy of 14.7 kJ mol^{-1}[3].

We have performed an X-ray structure analysis on dimethyl 1,2-heptalenedicarboxylate *(2)*[4] which is stabilized by ester groups and has been synthesized by *Hafner* and *Diehl*. Compound *(2)* forms monoclinic red leaflets of m. p. 114—115 °C; $a = 1242 \pm 1$, $b = 818 \pm 1$, $c = 1396 \pm 1$ pm, $\beta = 105.14 \pm 0.05°$, $V_{UC} = 1370 \times 10^6$ pm^3, $Z = 4$, $d_{X\text{-ray}} = 1.310$ g cm^{-3}, $d_{exp} = 1.315$ g cm^{-3}, space group $P2_1/a$.

2160 reflections *hkl* ($0 \le k \le 6$) have been measured with $Cu_{K\alpha}$ radiation ($\lambda = 1.5418$ Å) on a two-circle diffractometer. The structure was solved and refined ($R = 0.098$) with the program system of *Sheldrick*[5].

The heptalene system in *(2)* (Fig. 1a) consists of two boat-shaped seven-membered rings with structural angles of $\alpha = 36.8°$, $\beta = 22.0°$ (substituted ring) and $\alpha = 37.3°$, $\beta = 22.7°$. Although smaller than in other seven-membered rings with three localized double bonds[6], these structural angles nevertheless lead to pronounced deformation of the bicyclic system. The ester groups are twisted by 30° (position 1) and 25° (position 2) relative to the ring. They are arranged in such a way that the slightest mutual approach will lead to maximal

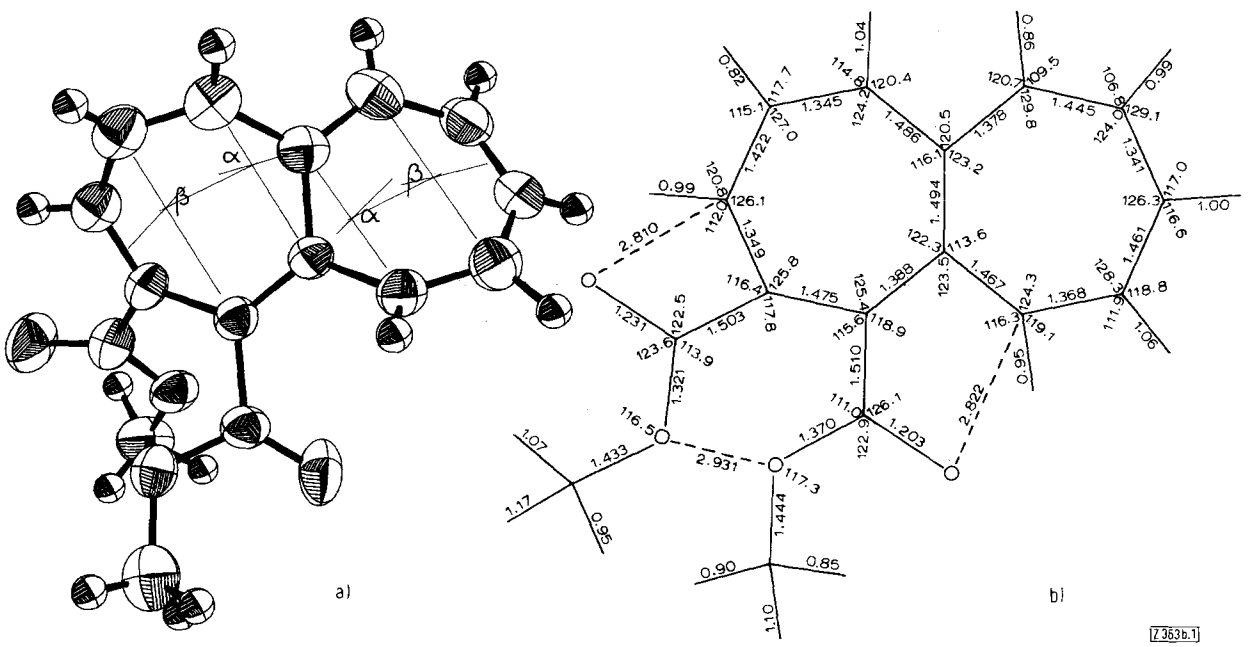

Fig. 1. a) Molecular structure of *(2)*; b) bond lengths and angles (bond lengths in 10^2 pm). Standard deviations: $\sigma_{XX} = 0.8$ pm; $\sigma_{XH} = 7$ pm; $\sigma_{XXX} = 0.5°$; $\sigma_{XXH} = 3.0°$ (X = C, O).

Crystal and Molecular Structure of Dimethyl 1,2-Heptalenedicarboxylate[**]

By *Hans Jörg Lindner* and *Brigitte Kitschke*[*]

Theoretical studies have shown that the localized heptalene structure *(1a)* is energetically preferred over the delocalized structure *(1b)*[1]. *Bertelli* deduced a nonplanar structure of conjugative interaction with the ring system. The bond lengths and angles (Fig. 1b) show an alternance already apparent from the form of the heptalene system.

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Angew. Chem. 86, 777 (1974); Angew. Chem. Int. Ed. Engl. 13, 732 (1974); E. Vogel and J. Ippen, Angew. Chem. 86, 778 (1974); Angew. Chem. Int. Ed. Engl. 13, 734 (1974); E. Vogel and F. Hogrefe, Angew. Chem. 86, 779 (1974); Angew. Chem. Int. Ed. Engl. 13, 735 (1974).
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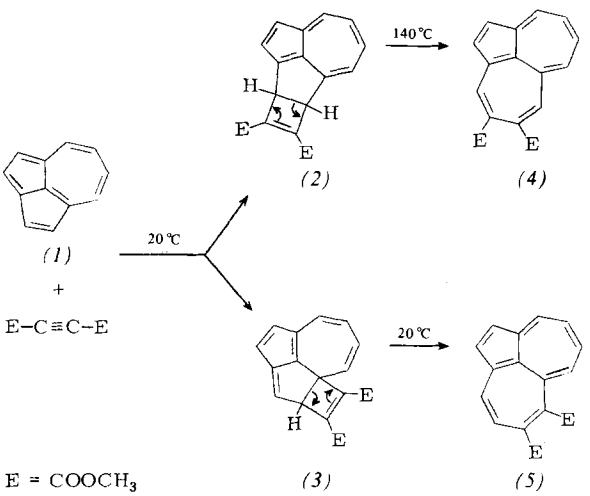
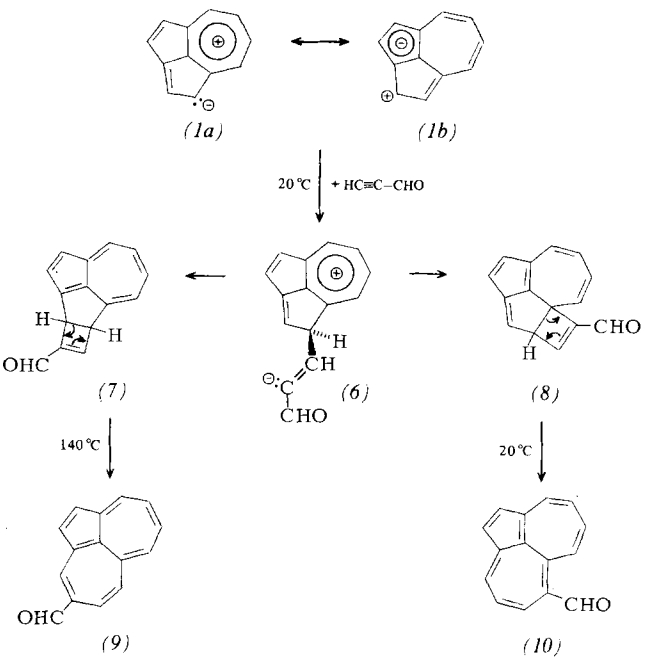
1,4-Dipolar Cycloadditions of Cyclopent[*cd*]azulene[**]

By *Herbert Diehl* and *Klaus Hafner*[*]

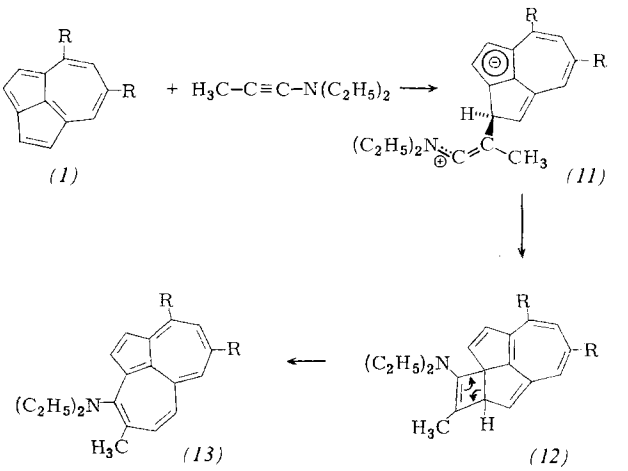
Cycloadditions of nonbenzenoid carbo- and heterocyclic conjugated π-electron systems with suitable reactants provide a facile entry to ring systems that were hitherto difficult to prepare, if at all[1]. For instance, cyclopent[*cd*]azulene *(1)*[2] which is now readily accessible reacts with dimethyl acetylenedicarboxylate even at room temperature to give 75% of the 1:1 adduct *(2)* (blue-green leaflets, m.p. 104—105 °C[3]; thermal valence isomerization thereof in boiling xylene yields 95% of dimethyl 4,5-aceheptylenedicarboxylate *(4)* (brown crystals, m.p. 97—98 °C). Formation of small amounts of the isomeric 5,6-diester *(5)* together with *(2)* is in agreement with results of our earlier studies[4]. Compound *(5)* presumably arises from the primary adduct *(3)* which appears to be unstable at as low a temperature as 20 °C. The formation of *(2)* and *(5)* suggests that cycloaddition of *(1)* with alkynes proceeds *via* a two-step mechanism involving a resonance-stabilized 1,4-dipole. The solvent dependence[5] of this cycloaddition and orientation phenomena observed in the reactions of *(1)* with electron-poor and electron-rich alkynes do corroborate this suggestion.



Compound *(1)* rapidly reacts with propiolaldehyde in dichloromethane at 20 °C *via* the primarily formed dipolar intermediate *(6)* to give the adducts *(7)* (yield 76%, blue oil) and *(8)*, which as a result of pronounced ring strain immediately undergoes valence isomerization to 3% of 6-aceheptylenecarbaldehyde *(10)*[6] (reddish brown needles, m.p. 65—66 °C). In contrast, *(7)* is only converted into the isomeric 4-carbaldehyde *(9)*[6] (90% yield, yellowish brown crystals, m.p. 75—76 °C) on heating to 140 °C (boiling xylene, 1 h).



However, *(1)* and its 5,7-dimethyl derivative (R = CH_3) combine with *N,N*-diethyl-1-propynylamine, according to the resonance structure *(1b)*, *via* the dipolar intermediate *(11)* (R = H or CH_3) to give exclusively the adduct *(12)* which immediately affords the aceheptylene derivative *(13)* (R = CH_3; yellowish brown oil, m.p. of the 1,3,5-trinitrobenzene derivative 173—174 °C) by cleavage of the cyclobutene ring[7].



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CAS Registry numbers:
(1), 209-86-9; *(2)*, 58150-77-9; *(3)*, 58150-78-0; *(4)*, 58150-79-1; *(5)*, 58150-80-4; *(7)*, 58150-81-5; *(8)*, 58150-82-6; *(9)*, 58150-83-7; *(10)*, 58150-84-8; *(12)* (R = CH_3), 58150-85-9; *(13)* (R = CH_3), 58150-86-0; dimethyl acetylenedicarboxylate, 762-42-5; propiolaldehyde, 624-67-9; *N,N*-diethyl-1-propynylamine, 4079-68-9; 5,7-dimethyl derivative of *(1)*, 58150-87-1

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

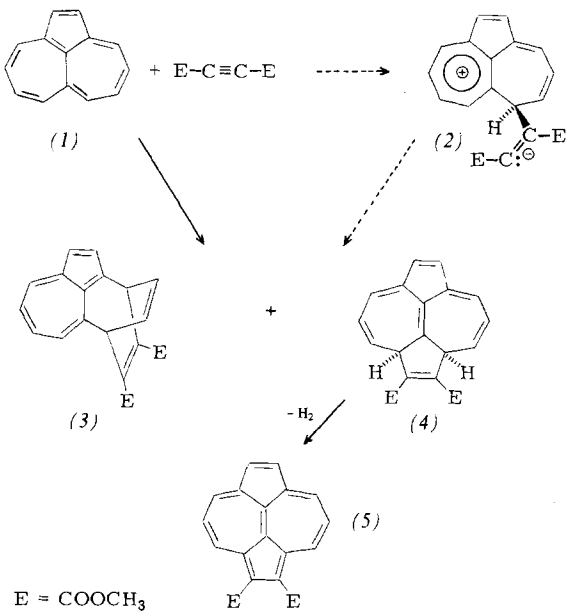
[1] K. Hafner, H. Diehl, and H. U. Süss, Angew. Chem. 88, 121 (1976); Angew. Chem. Int. Ed. Engl. 15, 104 (1976); cf. also K. Hafner, J. Häring, and W. Jäkel, Angew. Chem. 82, 132 (1970); Angew. Chem. Int. Ed. Engl. 9, 159 (1970); K. Hafner and W. Rieper, Angew. Chem. 82, 218 (1970); Angew. Chem. Int. Ed. Engl. 9, 248 (1970); K. Hafner, J. Heterocycl. Chem., in press.

[2] *K. Hafner, K.-P. Meinhardt*, and *W. Richarz*, Angew. Chem. *86*, 235 (1974); Angew. Chem. Int. Ed. Engl. *13*, 204 (1974).
[3] Structures of all compounds described were confirmed by elemental analysis, UV, NMR, and MS spectra.
[4] *K. Hafner* and *R. Fleischer*, Angew. Chem. *82*, 217 (1970); Angew. Chem. Int. Ed. Engl. *9*, 247 (1970); *K. Hafner*, Pure Appl. Chem. *28*, 153 (1971).
[5] *H. Diehl*, Dissertation, Technische Hochschule Darmstadt, 1976.
[6] *(9)* and *(10)* can be obtained in 27 and 12% yield together with 1-aceheptylenecarbaldehyde (55%) by direct Vilsmeier formylation of aceheptylene with dimethylformamide/phosphoryl chloride.
[7] The compound *(13)*, R = H, arising from *(1)*, R = H, rapidly undergoes further cycloaddition with the ynamine to form 3-diethylamino-4,10-dimethylbenzo[*a*]cyclopent[*cd*]azulene (green leaflets, m.p. 97 °C); cf. *K. Hafner, H. Diehl*, and *W. Richarz*, Angew. Chem. *88*, 125 (1976); Angew. Chem. Int. Ed. Engl. *15*, 108 (1976).

Cycloadditions of Aceheptylene—A Facile Synthesis of Dicyclopenta[*ef,kl*]heptalenes[**]

By *Klaus Hafner, Herbert Diehl*, and *Winfried Richarz*[*]

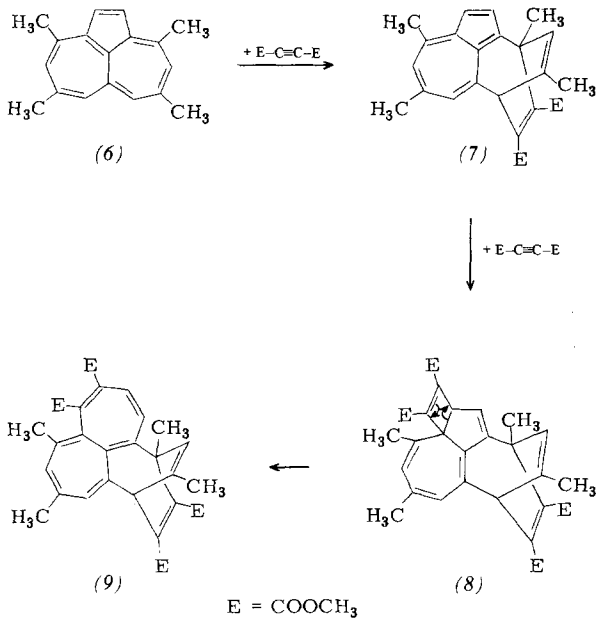
Similarly to pentalene, azulene[1], and cyclopent[*cd*]azulene[2], the readily accessible aceheptylene *(1)*[3] undergoes



cycloaddition with activated alkynes to form novel polycyclic systems in a surprisingly simple manner.

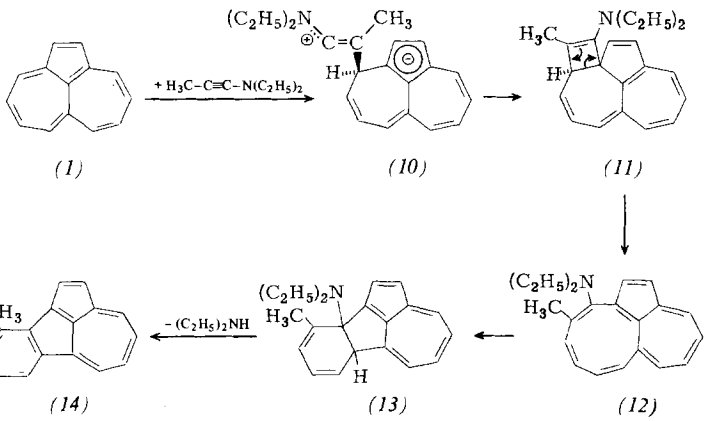
Heating of *(1)* with dimethyl acetylenedicarboxylate in the molar ratio 1:1 in boiling tetralin for 1 h affords 25% of dimethyl 1,2-dicyclopenta[*ef,kl*]heptalenedicarboxylate *(5)* (yellowish brown needles, m.p. 172—173 °C) along with 1% of the Diels-Alder adduct *(3)* (blue-green crystals, m.p. 100—101 °C)[4, 5]. Compound *(5)* presumably results from the primary adduct *(4)*, which like *(3)* can be formed from the dipolar intermediate *(2)* produced on attack by the electron-poor alkyne at the position of highest electron density in *(1)*, or by synchronous cycloaddition. 3,5-Dimethyl-[4] and 3,5,8,10-tetramethylaceheptylene *(6)*[6] also react with the acetylenic ester in a manner analogous to *(1)*, although formation of the Diels-Alder adducts of type *(3)* predominates. The parent tetracyclic system of *(5)* was hitherto accessible in only very low overall yield by multistep syntheses[7]. The spectroscopic properties of *(5)* resemble those of the unsubstituted tetracyclic hydrocarbon as far as comparison is at all justified.

Like azulene, the azulenoid Diels-Alder adducts of type *(3)* undergo a dipolar cycloaddition across positions 1,8a of the azulenoid partial structure on treatment with dimethyl acetylenedicarboxylate. Thus 3,5,8,10-tetramethylaceheptylene *(6)*[6], an electron-rich derivative of *(1)*, reacts with



the acetylenic ester in the molar ratio 1:2 to give 3% of the 3,5,8,10-tetramethyl derivative of *(5)* (light brown needles, m.p. 222 °C), 26% of the Diels-Alder adduct *(7)* (blue green crystals, m.p. 142—143 °C), and 12% of the thermally stable diene adduct of the unknown cyclohepta[*ef*]heptalene *(9)* (orange needles, m.p. 205—206 °C; UV spectrum (dioxane): $\lambda_{max} = 280$ ($\log\varepsilon = 4.16$), 292 (4.17), 347 (3.53), 426 (3.15)). The primary formation of the 1:1 adduct *(7)* is followed by a second cycloaddition to give the adduct *(8)*, valence isomerization of which, *via* cyclobutene ring opening, yields *(9)*.

Compound *(1)* and its derivatives also react with ynamines in unexpectedly high yields *via* cycloaddition; however, the electron-rich alkyne initially attacks the position of lowest electron density. Reaction of *(1)* with *N,N*-diethyl-1-propynylamine leads presumably *via* the dipolar intermediate *(10)*



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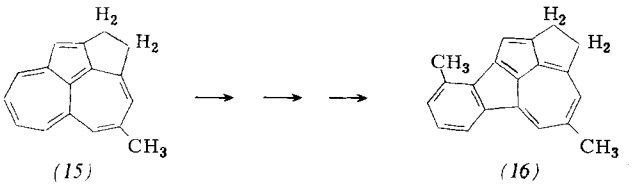
and the cycloadduct *(11)* to the thermally unstable cyclonona[*cd*]azulene derivative *(12)* resulting in cyclobutene ring opening; renewed valence isomerization of *(12)* to *(13)* and subsequent elimination of diethylamine affords a 75% yield of the hitherto inaccessible 10-methylbenzo[*a*]cyclopent[*cd*]azulene *(14)* (yellow-brown platelets, m.p. 136—



(15) *(16)*

137 °C)[8]. In analogous manner, the tetracyclic hydrocarbon *(15)* can be transformed in 21% yield into 4,9-dimethyl-1,2-dihydrobenzo[1,2]dicyclopent[*cd,ij*]azulene *(16)* (bronze colored needles, m.p. 144 °C).

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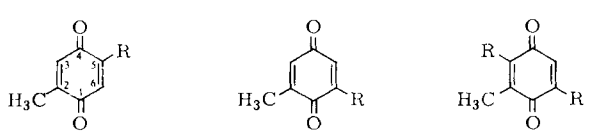
CAS Registry numbers:
(1), 209-42-7; *(3)*, 58150-65-5; *(4)*, 58150-66-6; *(5)*, 58150-67-7; *(5)*, 3,5,8,10-tetramethyl derivative, 58150-68-8; *(6)*, 17597-70-5; *(7)*, 58150-69-9; *(8)*, 58150-70-2; *(9)*, 58150-71-3; *(11)*, 58150-72-4; *(12)*, 58150-73-5; *(13)*, 58150-74-6; *(14)*, 58150-75-7; *(15)*, 1143-34-6; *(16)*, 58150-76-8; dimethyl acetylenedicarboxylate, 762-42-5; *N,N*-diethyl-1-propynylamine, 4079-68-9

[1] *K. Hafner, H. Diehl*, and *H. U. Süss*, Angew. Chem. *88*, 121 (1976); Angew. Chem. Int. Ed. Engl. *15*, 104 (1976).
[2] *H. Diehl* and *K. Hafner*, Angew. Chem. *88*, 124 (1976); Angew. Chem. Int. Ed. Engl. *15*, 107 (1976).
[3] *K. Hafner*. Pure Appl. Chem. *28*, 153 (1971).
[4] *(1)* and its alkyl derivatives also undergo Diels-Alder reaction with maleic anhydride and tetracyanoethylene; *K. Hafner* and *J. Schneider*, Justus Liebigs Ann. Chem. *624*, 37 (1959); *K. Hafner* and *G. Schneider*, *ibid. 672*, 194 (1964).
[5] Correct elemental analyses, UV, NMR, and MS spectra were obtained for all compounds described.
[6] Cf. [3] and *K. Hafner, G. Hafner-Schneider*, and *F. Bauer*, Angew. Chem. *80*, 801 (1968); Angew. Chem. Int. Ed. Engl. *7*, 808 (1968).
[7] *A. G. Anderson, Jr., A. F. Montana, A. A. MacDonald*, and *G. M. Masada*, J. Org. Chem. *38*, 1445 (1973); *Ch. Jutz* and *E. Schweiger*, Synthesis *1974*, 193.
[8] 3,5-Dimethyl- [4] and 3,5,8,10-tetramethylaceheptylene *(6)* [6] react with *N,N*-diethyl-1-propynylamine to give 68% of 3,5-dimethyl- and 92% of the 3,5,7,9-tetramethyl derivative, respectively, of *(14)*.

Oxidative Amination of Toluhydroquinone[**]

By *Suresh C. Srivastava* and *Ulfert Hornemann*[*]

Schäfer and *Aguado*[1] have reported that the interaction of a variety of hydroquinones with arylamines and sodium iodate constitutes a facile route for the preparation of bis(arylamino)-1,4-benzoquinones including *(3)*, for which they gave



(1), R = NHC_6H_5 *(2)*, R = NHC_6H_5 *(3)*, R = NHC_6H_5
(4), R = OH *(5)*, R = OH *(6)*, R = OH

a decomposition point of 147 °C but no data to prove its structure. During our attempts to prepare 3,6-dianilinotoluquinone *(3)* by this route using 10 mmol of toluhydroquinone, 20 mmol of aniline (each dissolved in 75 ml of methanol) and 30 mmol of sodium iodate (dissolved in 75 ml of water) and stirring the mixture for 24 h at room temperature, we observed that the predominant reaction product is 5-anilinotoluquinone *(1)* (50% yield), that *(3)* is obtained in only 26% yield, and that the novel 6-anilinotoluquinone *(2)* is formed in 10% yield.

(1) is also the predominant or a major reaction product when the relative amounts of the reactants are varied. With 10 instead of 20 mmol of aniline the yields of *(1)*, *(2)* and *(3)* are 70%, 15% and 10%, respectively, while when 30 mmol instead of 10 mmol of toluhydroquinone is used the yields of *(1)* and *(2)* are 40% and 50%, respectively, and no *(3)* can be detected. In contrast to these observations, but presumably in accord with results obtained by *Zincke*[2], it was found that a reaction mixture containing 30 mmol toluquinone and 20 mmol aniline in ethanol yielded *(1)* and *(3)* in 60% and 30% yield, respectively, and no detectable quantity of *(2)*.

The composition of the reaction mixtures in most cases is 50—70% of *(1)* *versus* 30—50% of *(2)* plus *(3)*. This may be explained as follows: Assuming that it is the sole function of the iodate to generate toluquinone, the product ratio reflects the difference in the reactivity of position 5 *versus* 6 of toluquinone towards attack by the nucleophilic aniline. Moreover, once any *(2)* has formed it can give rise to *(3)* and the extent of this conversion is dependent on the amount of aniline and the amount of oxidizing agent present in the reaction mixture. This explanation holds for most of the reaction mixtures except for that in which toluhydroquinone and sodium iodate were used in excess of aniline. The observed increase in the amount of *(2)* formed in this case is reproducible but is not readily explained. We suggest that partial formation of a quinhydrone, which would be expected to have the methyl groups oriented in a "*para*" arrangement, may lead to increased accessibility of the 6 position.

Table 1. Physical data for compounds *(1)* to *(6)*. All compounds gave the molecular ion in the mass spectrum.

Cpd.	M.p. [°C] (dec.)	^{1}H-NMR (δ values, in $CDCl_3$)
(1)	150—151	2.05 (d, 3H, J_{23} = 1.5 Hz), 6.13 (s, 1H), 6.52 (br., 1H), 7.24 (br., 5H)
(2)	155—156	2.12 (d, 3H, J_{23} = 2.0 Hz), 6.18 (d, 1H, J_{35} = 2.5 Hz), 6.58 (m, 1H), 7.32 (br., 5H)
(3)	240—242	1.59 (s, 3H), 6.03 (s, 1H), 7.30 (br., 10H)
(4)	127—141	2.03 (d, 3H, J_{23} = 1.5 Hz), 6.05 (s, 1H), 6.60 (br., 1H)
(5)	110—120 [a]	2.10 (d, 3H, J_{23} = 1.5 Hz), 6.20 (d, 1H, J_{35} = 2.0 Hz) 6.60 (m, 1H)
(6)	166—171 [b]	1.97 (s, 3H), 7.24 (s, 1H)

[a] M.p. 117—127 °C (dec.) [5]; [b] M.p. 173—175 °C [6].

3,6-Dianilinotoluquinone *(3)* (Table 1) precipitated from the reaction mixture as a yellow brown powder and was recrystallized from chloroform; the compound is presumably identical with the dianilinotoluquinone (m.p. 232—233 °C) prepared by *Zincke*[2]. The filtrate obtained after removal of *(3)* was evaporated to dryness, the residue extracted with methanol and the extract concentrated to yield *(1)* (Table 1) as red crystals; this material is presumably identical with the reaction product obtained by *Schäfer* and *Aguado*[1] and with *Zincke's* monoanilinotoluquinone, (m.p. 144—145 °C). *(2)* (Table 1) was obtained as red crystals after chromatography of the mother liquor on a silica gel column which was

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developed with chloroform. The ^{1}H-NMR spectra of *(1)*—*(3)* are in accord with the proposed structures (cf. [3]).

Further proof for the identity of the anilinoquinones *(1)*—*(3)* was obtained by converting them into the known hydroxyquinones *(4)*[4], *(5)*[5] and *(6)*[6], respectively, with refluxing 10% H_2SO_4/methanol (1:1) for 10 min (Table 1). Each reaction mixture was poured into water, the product extracted with chloroform, the chloroform layer dried with Na_2SO_4 before evaporation, and the resulting hydroxyquinones purified by sublimation.

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CAS Registry numbers:
(1), 57674-09-9; *(2)*, 57674-10-2; *(3)*, 21111-68-2; *(4)*, 615-91-8; *(5)*, 2446-75-5; *(6)*, 2207-58-1

[1] *W. Schäfer* and *A. Aguado*, Angew. Chem. *83*, 441 (1971); Angew. Chem. Int. Ed. Engl. *10*, 405 (1971).
[2] *T. Zincke*, Ber. Dtsch. Chem. Ges. *16*, 1555 (1883).
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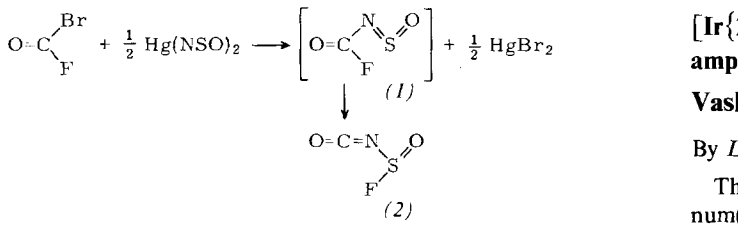
Fluorosulfinyl Isocyanate[**]

By *Hans-Joachim Krannich* and *Wolfgang Sundermeyer*[*]

All previous attempts to prepare halosulfonyl pseudohalides, OSXY, and sulfinyl bispseudohalides, OSY_2 (X = halogen; Y = pseudohalogen) have failed[1]. We have now succeeded in synthesizing the first compound of type OSXY by reaction of fluorocarbonyl bromide[2] with bis(sulfonylamido)mercury(II)[3]. The fluorosulfinyl isocyanate *(2)* is formed in a rearrangement reaction—to our knowledge formerly unobserved—from the expected intermediary fluorocarbonylsulfinylamine *(1)*; the CF bond becomes an SF bond.



OCFBr (*ca.* 27 g) is condensed *via* a high-vacuum apparatus onto $Hg(NSO)_2$ (5.1 g) in a 200 ml Duran glass ampoule; the ampoule is then sealed and shaken for 48 h at 10—15 °C. After removal of the volatile reaction products in a high vacuum the excess OCFBr serving as reaction medium is separated from the product at normal pressure for further use. The combined product after five such treatments afforded 4.5 g of *(2)* (yield 26.7%) as an almost colorless liquid (b. p. 60.5 °C) which slowly turns yellow at room temperature.

While elemental analysis merely affords evidence of the presence of *(1)* or *(2)*, the mass spectrum clearly indicates presence of the isomer *(2)*: $m/e = 109$ molecular ion (rel. int. 57.8%), 90 OS—NCO (12.5), 67 OSF (100), 64 SO_2 (6.3), 48 SO (25), 46 NS (18.8), 42 NCO (14.0), and 32 S (7.8); the transition 109→67 is evidenced by a metastable peak at 41 (calc. 41.18). The ^{19}F-NMR spectrum shows a singlet at −55.5 ppm ($CFCl_3$ ext. standard), which can be attributed to an OSF bond in contrast to an OCF bond[4] (for comparison: CH_3O—S(O)F (−55.6 ppm)[5a], $(CF_3)_2N$—O—S(O)F (−59.5 ppm[5b]). In the IR spectrum there are no carbonyl bands. Bands do occur, however, at 2245 (vs, ν_{as}NCO), 2192 (m, sh), 1348 (s, ν_sNCO), 1281 (vs, νSO), 753 (vs, νSF), 716 (vs, νSN), 610 (vs, δNCO), and 488 cm^{-1} (m) (gas spectrum). Also present is the combination band of the two NCO vibrations at *ca.* 3580 cm^{-1}. In the Raman spectrum the intensity ratio of the two NCO bands is typically reversed.

Our redistribution experiments on carbonyl halides and pseudohalides[6] indicate a relatively high mobility of the fluorine atom in the neighborhood of a carbonyl group. An intermolecular exchange of the fluorine atom between the two C atoms, observable in the case of fluorocarbonyl isocyanate OC(F)NCO by a broad ^{19}F-NMR signal at room temperature[7], leads in the case of *(1)* to an irreversible rearrangement to *(2)*.

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CAS Registry numbers:
OCFBr, 753-56-0; $Hg(NSO)_2$, 25682-06-8; fluorosulfinyl isocyanate, 57789-32-9

[1] *G. Jander* and *D. Ullmann*, Z. Anorg. Allg. Chem. *230*, 405 (1937); *G. S. Forbes* and *H. H. Anderson*, J. Am. Chem. Soc. *65*, 2271 (1943); *P. W. Schenk* and *H. Bloching*, Chem. Ber. *92*, 2333 (1959).
[2] *G. Siegemund*, Angew. Chem. *85*, 982 (1973); Angew. Chem. Int. Ed. Engl. *12*, 918 (1973).
[3] *W. Verbeek* and *W. Sundermeyer*, Angew. Chem. *81*, 330 (1969); Angew. Chem. Int. Ed. Engl. *8*, 376 (1969).
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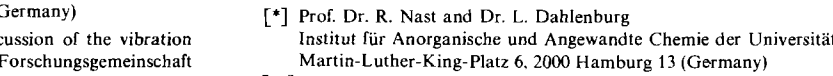
[Ir{2,4,6-$C_6H_2(CH_3)_3$}(CO)(PPh_3)$_2$]—The First Example of *cis-trans* Isomerism in Complexes of the Vaska Type[**]

By *Lutz Dahlenburg* and *Reinhard Nast*[*]

The *cis-trans* isomerism frequently found in planar platinum(II) complexes of the type $[Pt(L)_2(X)(Y)]$ has so far not been observed in the numerous comparable iridium(I) complexes of the Vaska type $IrA(CO)L_2$ (A = univalent anion ligand, L = tertiary phosphane or arsane). On the basis of their ^{1}H- and ^{31}P-NMR spectra and their dipole moments all these compounds prove to have a *trans* configuration, which, in two cases [A, L = Cl, P(*o*-$C_6H_4CH_3)_3$; C_6F_5, P($C_6H_5)_3$] has also been confirmed by X-ray structure analysis[1, 2]. The postulated existence of *cis*-[$IrA(CO)(PPh_3)_2$] [A = H, $C(CN)_3$] is doubtful[3], if not already ruled out[4].

We are now able to show that the σ-mesityl complex *(2)*, which is accessible according to



Mes = 2,4,6-$C_6H_2(CH_3)_3$

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Table 1. Spectroscopic data for the *cis*- and *trans*-forms of the complex *(2)*.

	(2a)	*(2b)*	Assignment
Typical IR bands			
[cm^{-1}] [a]	2950—2850 w	2980—2870 w	$\nu(CH_3)$
	1954 vs	1949 vs	$\nu(CO)$
	841 s	841 s	γ(mesityl-H)
	1973 vs	1941 vs	$\nu(CO)$ [b]
$\tau(^1H)$ [ppm] [c]	2.37—3.06 (M)	2.43—2.88 (M)	30 phenyl-H
	3.57 (S)	4.05 (S)	2 mesityl-H
	7.65 (S)	8.41 (S)	6 methyl-H
	7.93 (S)	8.08 (S)	3 methyl-H
$\delta(^{31}P)$ [ppm] [d]	−26.23, −21.11 [e]	−22.82 (S)	

[a] KBr pellet. [b] $CHCl_3$ solution. [c] 60 MHz, $CDCl_3$, TMS internal. [d] 24.29 MHz, C_6D_6, 85% H_3PO_4 external. [e] AB spectrum, J(PIrP) = 22.0 Hz.

consists of an easily separable 10:1 mixture of red *cis-(2a)* and yellow *trans*-form *(2b)*. The identification and purity of the two isomers was confirmed by elemental analysis and molecular weight determination[5] as well as by IR and ^{1}H-NMR spectra (cf. Table 1).

While solutions of pure *(2a)* in chloroform or benzene show no tendency whatsoever to undergo the rearrangement *(2a)* → *(2b)*, complete *cis-trans* isomerization is observed to take place within 24 h in the presence of catalytic amounts of PPh_3. Hence, we consider *(2a)* as the kinetically hindered unstable form and *(2b)* as the thermodynamically stable form.

The configuration of the two isomers follows from the findings listed below:

1. Only the singlet signal expected for the *trans*-grouping P—Ir—P appears in the ^{31}P-NMR spectrum of *(2b)*; *(2a)*, on the other hand, shows the AB spectrum required by *cis* phosphane ligands (Table 1).

2. The measured (benzene, 25 °C) and calculated electric dipole moments (assuming the atomic polarization as 20% of the electron polarization) with values of 6.5 D for *(2a)* and 1.7 D for *(2b)* lie in the range expected for *cis* and *trans* configurations of these complexes respectively[6].

3. The ν(CO) wave numbers (Table 1) measured in $CHCl_3$ are also in agreement with this assignment of configuration, since the doubtless larger σ-donor/π-acceptor ratio of the anionic mesityl group compared to the neutral ligand PPh_3 must influence the ν(CO) values of *trans*-OC-Ir-PPh_3 in *(2a)* and of *trans*-OC-Ir-Mes in *(2b)* in the observed sense.

The isolation of the red mesityl complex *(2a)* affords the first unequivocal proof of the—doubtless sterically determined—existence also of *cis*-configurated compounds of the Vaska type.

Experimental:

A mixture of *(1)* (7.80 g, 0.010 mol) and mesityllithium (0.015 mol) in diethyl ether (1500 ml) is stirred at room temperature for 2 h under protective gas (N_2). After filtration and addition of ethanol (200 ml) the ether is removed by evaporation at normal pressure. Crystallization of red *(2a)* ensues and is practically complete after 6–8 h at room temperature. Yield (after washing with 3 × 20 ml ethanol) 4.7–5.4 g (55–65%).—Approximately 500 mg yellow *(2b)* crystallizes from the mother liquor within a week at 0 °C. Traces of the *cis* complex disappear if *ca.* 1 g portions of the impure crystals are stirred together with 50 mg PPh_3 in 50 ml benzene; concentration of the solution to 10 ml and addition of 10 ml hexane leads to crystallization of the pure *trans* complex *(2b)*.—Pure *(2a)* can be transformed into *(2b)* in 85% yield by the same method.

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CAS Registry numbers:
mesityllithium, 5806-59-7; *(1)*, 14871-41-1; *(2a)*, 58207-12-8; *(2b)*, 58207-13-9

[1] *W. H. De Camp, M. L. Schneider, J. D. Scott, J. M. Stewart* and *L. Vaska*, 164th National Meeting Am. Chem. Soc., New York 1972, Pap. INOR 98.
[2] *R. Gopal* and *A. Clearfield*, Abstr. Pap. Am. Chem. Soc., Summer Meeting, E 11, 230 (1974).
[3] *G. Yagupsky* and *G. Wilkinson*, J. Chem. Soc. *A 1969*, 725.
[4] *W. Beck, K. Schorpp, C. Oetker, R. Schlodder*, and *H. S. Smedal*, Chem. Ber. *106*, 2144 (1973).
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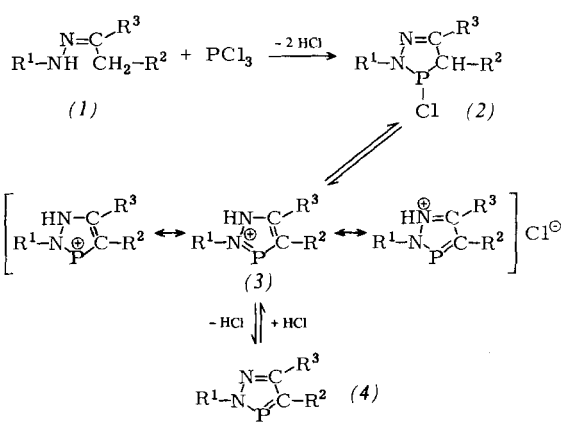
First Example of a Chlorophosphane→Phosphanylium Chloride Transformation: 2-Methyl-1,2,3σ^2-diazaphosphole Hydrochlorides[1]

By *Jörg Luber* and *Alfred Schmidpeter*[*]

The reaction of the hydrazones *(1)* with phosphorus trichloride, which leads by elimination of 3 mol. equiv. of hydrogen chloride to 2*H*-1,2,3σ^2-diazaphospholes *(4)* ($R^1 \neq CH_3$[2]), should proceed *via* 3-chloro-Δ^5-1,2,3σ^3-diazaphospholines *(2)* as intermediates. In two cases these intermediates have actually been isolated ($R^1 = CH_3CO$ or *p*-$CH_3C_6H_4$, $R^2 = H$, $R^3 = CH_3$)[3].

We have now investigated the hitherto unelucidated[4] reaction of methylhydrazones *(1)*, $R^1 = CH_3$, under modified conditions and thus obtained crystalline products *(3)* corresponding to *(2)* in their composition, yet ionic in nature. They are apparently formed from *(2)* by extrusion of the chlorine as an anion leaving a twofold coordinated phosphorus atom in the cyclic cation. The compounds are therefore to be regarded as "phosphenium chlorides" (phosphanylium chlo-



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rides) and provide the first example of this kind of isomerization[5].

As a result of the proton shift the phosphenium charge in *(3)* can also be distributed over the two nitrogen ring members. However, as is shown by a comparison with the strongly Lewis acidic diaminophosphenium ions[5], this charge distribution alone is inadequate to explain the spontaneous formation of *(3)*. It can be rationalized by the formation of the cyclic 6π-electron system in the cation.

The ionic structure *(3)* and the proton shift are confirmed by the very broad IR band at about 2300 cm^{-1} due to an $NH^+\cdots Cl^-$ hydrogen bond, by the large downfield shift in the ^{31}P-NMR spectrum (Table 1) characteristic of twofold coordinated phosphorus, and by the absence of a proton in position 4 of *(3b)*. Reaction with $HgCl_2$ affords the chloromercurates *((3)*, $HgCl_3$ instead of Cl) whose IR spectrum indicates an unchanged structure.

In the NMR spectrum of *(3a)* the proton on C^4 gives rise to a signal exhibiting a pronounced downfield shift and an exceptionally large coupling constant J_{PCH}, as is also observed in the case of *(4a)* and for the 2,6-protons of σ^2-phosphorine (phosphabenzene, 8.6 ppm and 38 Hz)[6]. This characterizes compounds *(3)* as σ^2-phospha-aromatics (phosphapyrazole hydrochlorides) and clearly distinguishes them from the isomers *(2)* (cf. Table 1).

The hydrochlorides *(3a, b)* readily afford *(4a, b)* so that 1,2,3σ^2-diazaphospholes with $R^1=CH_3$ are now also accessible. Treatment with HCl regenerates the hydrochlorides *(3)*.

In order to prepare the diazaphospholes *(4)* a slurry of hydrochloride *(3)* (25 mmol) in dry benzene (20 ml) is cooled on ice and treated with triethylamine (2.5 g, 25 mmol) in benzene (10 ml) with stirring. Triethylammonium chloride is separated off after 2 h, the benzene evaporated off *in vacuo*, and the residue distilled (yield 60—80 %).

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[1] Four- and Five-Membered Phosphorus Heterocycles, Part 12. This work was supported by the Deutsche Forschungsgemeinschaft.—Part 11: *W. S. Sheldrick, A. Schmidpeter*, and *J. H. Weinmaier*, Angew. Chem. *87*, 519 (1975); Angew. Chem. Int. Ed. Engl. *14*, 490 (1975).

[2] *A. F. Vasilev, L. V. Vilkov, N. P. Ignatova, N. N. Melnikov, V. V. Negrebetskii, N. I. Shvetsov-Shilovskii*, and *L. S. Khaikin*, J. Prakt. Chem. *314*, 806 (1972).

[3] With $R^1=CH_3C_6H_4$ the compound was obtained in only 5 % yield and not characterized further. *N. I. Shvetsov-Shilovskii, N. P. Ignatova*, and *N. N. Melnikov*, Zh. Obshch. Khim. *40*, 1501 (1970).

[4] N. I. *Shvetsov-Shilovskii, N. P. Ignatova, R. G. Bobkova, V. Ya. Manykhina*, and *N. N. Melnikov*, Zh. Obshch. Khim. *42*, 1939 (1972).

[5] Although diaminophosphenium ions have been reported, they can only be generated from diaminohalophosphanes with particularly strong halide acceptors and are only stable with $AlCl_4^-$, $B_2F_7^-$, or PF_6^- (sometimes also PCl_6^-) as counterions: *S. Fleming, M. K. Lupton*, and *K. Jekot*, Inorg. Chem. *11*, 2534 (1972); *B. E. Maryanoff* and *R. O. Hutchins*, J. Org. Chem. *37*, 3475 (1972); *M. G. Thomas, R. W. Kopp, C. W. Schultz*, and *R. W. Parry*, J. Am. Chem. Soc. *96*, 2646 (1974). The sole other phosphenium ions known, the phosphamethinecyanines, are only accessible with BF_4^- or ClO_4^- as anion: *K. Dimroth*, Fortschr. Chem. Forsch. *38*, 1 (1973).

[6] *A. J. Ashe, III*, J. Am. Chem. Soc. *93*, 3293, 6690 (1971).

Table 1. Data for 1,2,3σ^2-diazaphospholes *(4)*, their hydrochlorides *(3)*, and a 3-chloro-1,2,3σ^3-diazaphospholine *(2)* for comparison (δ values in ppm, *J* values in Hz).

		(3a)	*(3b)*	*(4a)* [a]	*(4b)*	*(2)* [3]
	R^1	CH_3	CH_3	CH_3	CH_3	CH_3CO
	R^2, R^3	H, CH_3	$(CH_2)_3$	H, CH_3	$(CH_2)_3$	H, CH_3
M.p. [°C] or b.p. [°C/torr]		133—134	114—115	73/58	82/10	52—54
	$\delta^{31}P$	−230.7	−209.3	−228.9	−204.4	−110.9
R^1:	$\delta H(NCH_3)$	4.40	4.34	3.66	3.99	—
	J_{PNCH}	8.2	8.7	7.6	7.8	—
R^2:	$\delta^1H(CH_n)$	7.92	—	7.25	—	3.02
	J_{PCH}	39.1	—	43.7	—	24.0
R^3:	$\delta^1H(CCH_3)$	2.68	—	2.33	—	
	J_{PCCCH}	1.5	—	1.3	—	
M.p. [°C] of the chloromercurates *(3)*, $HgCl_3$ in place of Cl		117—119	98—99			

[a] Neat, otherwise in $CDCl_3$ solution.

Owing to the low basicity of *(4)*, the hydrochlorides *(3)* undergo thermal dissociation and are sublimable *via* a dissociation equilibrium. The mass spectra of *(3)* always contain the molecular ion of *(4)* as the peak of highest mass and greatest intensity.

Procedures:

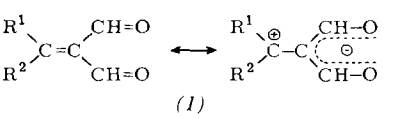
All reactions are carried out under an inert gas (argon). An *N*-methylhydrazone (50 mmol) is added dropwise over 15 min to stirred PCl_3 (34.3 g, 250 mmol) cooled to −30 to −60 °C. After slowly warming to room temperature the mixture is refluxed for 2 h. The hydrochloride *(3)* which crystallizes on cooling is collected on a frit and washed with ether. It is best purified by sublimation at 40—60 °C and reduced pressure or slowly even at atmospheric pressure; yield 55 % *(3a)* and 40 % *(3b)*.

For conversion into the chloromercurates ($HgCl_3$ in place of Cl), compound *(3)* (10 mmol) is dissolved in dry acetonitrile (20 ml) and a solution of $HgCl_2$ (2.7 g, 10 mmol) in acetonitrile (10 ml) is added. The crystals precipitating within 24 h are analytically pure after drying (yield 80 %).

Synthesis of Alkylidenemalondialdehyde Tetramethyl Bisacetals[1]

By *Christian Reichardt, Wilfried Pressler*, and *Ernst-Ulrich Würthwein*[*]

Alkylidenemalondialdehydes of the general formula *(1)* are not only of theoretical interest because of their cross-conju-



(1)

gated π-electron system, but are also (with $R^1=H$ and $R^2=CO_2R$) valuable intermediates in the synthesis of cephalosporin C[2]. The method described by *Woodward et al.*—aldol addition of the sodium salt of malondialdehyde to mesoxalates

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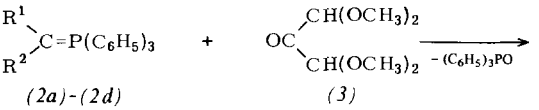
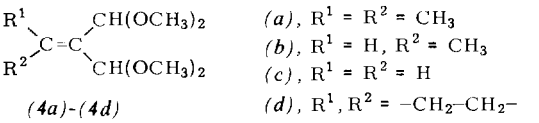
or glyoxylates and subsequent dehydration[2, 3]—is, however, unsuitable for the preparation of simpler alkylidenemalondialdehydes (with R^1, R^2=H or alkyl).—Introduction of two geminal formyl groups by Vilsmeier formylation meets with success only in special cases[4].

We have now found that the alkylidenemalondialdehyde tetramethyl bisacetals *(4a)*—*(4d)* can be prepared by Wittig olefination of the mesoxaldialdehyde tetramethyl bisacetal *(3)*[5] with the intermediary alkylidenetriphenylphosphoranes *(2a)*—*(2d)*.



(2a)-(2d) *(3)*



(4a)-(4d)

(a), $R^1 = R^2 = CH_3$
(b), $R^1 = H$, $R^2 = CH_3$
(c), $R^1 = R^2 = H$
(d), $R^1, R^2 = -CH_2-CH_2-$

For the synthesis of the cyclopropylidene compound *(4d)* the cyclopropylidenetriphenylphosphorane *(2d)*, obtained by reaction of an excess of the corresponding phosphonium salt[6] with potassium *tert*-butoxide in benzene, was heated under reflux for three days with *(3)*. Subsequent distillation afforded *(4d)* as a colorless liquid [b.p. 105—106 °C/12 torr, yield 89 % based on *(3)*; ^{1}H-NMR ($CDCl_3$): $\delta = 1.20$ (s, 4 cyclopropyl H), 3.32 (s, 12 OCH_3), and 4.90 ppm (s, 2 CH)].

The acetals *(4a)*—*(4c)* were obtained in 50, 38, and 26 % yield, respectively, on stirring a mixture of *(3)* 20 h at room temperature with the ylides *(2a)*—*(2c)*, prepared with phenyllithium in ether (see Experimental procedure). Subsequent distillation followed by preparative gas-chromatography of the crude products so obtained afforded analytically pure, colorless, readily volatile liquids whose elemental analyses, mass, IR, and ^{1}H-NMR spectra were consistent with the given constitutions. The compounds *(4a)*—*(4d)* are valuable starting substances for the synthesis of substituted malondialdehydes and heterocycles[7].

Isopropylidenemalondialdehyde tetramethyl bisacetal (4a)

An ethereal solution of phenyllithium, prepared by reaction of bromobenzene (13.0 g, 83 mmol) with lithium shavings (1.9 g, 274 mmol) in dry diethyl ether (150 ml), is added rapidly under N_2 to a suspension of isopropyltriphenylphosphonium bromide[8] (23.1 g, 60 mmol) in diethyl ether (200 ml). After one hours' stirring *(3)* (10.0 g, *ca.* 90 % pure, *ca.* 50 mmol) is added dropwise within 20 min. The viscous suspension is stirred for 20 h at room temperature; the solvent is then removed by distillation (maximum bath temperature 60 °C). The remaining yellow-brown hygroscopic solid is heated to 225 °C at *ca.* 0.2 torr, whereupon *(4a)* distils over at 55—57 °C/0.2 torr as crude product (8.0 g, *ca.* 65 % pure); overall yield [based on pure *(3)* and *(4a)*] *ca.* 50 %. Further purification of the product is accomplished by preparative gas chromatography (Perkin-Elmer F 21, 2 m × 23 mm column with 5 % SE-30 on Chromosorb G-NAW at 135 °C and a column feed-pressure of 1.6 kp/cm^2 N_2). ^{1}H-NMR ($CDCl_3$): $\delta = 1.88$ (s, 6 CH_3), 3.36 (s, 12 OCH_3), 4.85 ppm (s, 2 CH).

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(2a), 16666-80-1; *(2b)*, 1754-88-7; *(2c)*, 3487-44-3; *(2d)*, 14633-95-5; *(3)*, 19256-30-5; *(4a)*, 57842-93-0; *(4b)*, 57842-94-1; *(4c)*, 57842-95-2; *(4d)*, 57842-96-3

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[2] *R. B. Woodward*, Angew. Chem. *78*, 557 (1966); *R. B. Woodward, K. Heusler, J. Gosteli, P. Naegeli, W. Oppolzer, R. Ramage, S. Ranganathan*, and *H. Vorbrüggen*, J. Am. Chem. Soc. *88*, 852 (1966).
[3] *R. B. Woodward*, French Pat. 1495047 (1967); Chem. Abstr. *69*, 51640r (1968).
[4] *G. A. Reynolds* and *J. A. VanAllen*, J. Org. Chem. *34*, 2736 (1969); *V. Dressler* and *K. Bodendorf*, Arch. Pharm. (Weinheim) *303*, 481 (1970); *J. Čiernik*, Collect. Czech. Chem. Commun. *37*, 2273 (1972).
[5] *A. Maschke* and *H. Pasedach*, DBP 1905603 (1969), BASF; Chem. Abstr. *73*, 87436a (1970); cf. also *C. Reichardt* and *E.-U. Würthwein*, Synthesis, *1976*, in press.
[6] *H. J. Bestmann* and *E. Kranz*, Chem. Ber. *105*, 2098 (1972).
[7] *W. Pressler*, Dissertation, Universität Marburg 1975; *E.-U. Würthwein*, Dissertation, Universität Marburg 1975.
[8] *A. Maercker*, Org. React. *14*, 270 (1965), especially pp. 388 and 402ff.

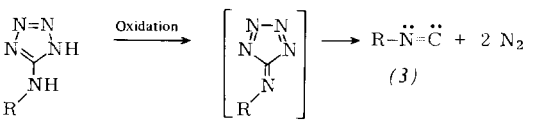
Oxidation of 5-Aminotetraazoles, a New Route to Isocyanides[**]

By *Gerhard Höfle* and *Bernd Lange*[*]

Attempts to prepare the unknown compounds R—CO—N̈=C̈[1] gave us cause to search for reagent-free isocyanide syntheses. The thermal or photochemical fragmentation of imino-substituted cyclic compounds according to the following scheme[2] appeared promising:

As concerted processes these reactions are not symmetry forbidden since the isocyanide fragment can be extruded in a linear or nonlinear manner[3]; they ought to proceed particularly easily provided particles X of low energy are formed.

We report here on a model reaction in which one molecule of isocyanide *(3)* and two molecules of nitrogen are formed from 5-iminotetrazoles *(2)* in a [2+2+2] cycloreversion. Starting materials for the synthesis of *(2)* were the 5-alkyl(aryl)-aminotetrazoles *(1)*, which are readily accessible from commercially available 5-aminotetrazole[4] or monosubstituted thioureas[5].



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

Oxidation of *(1a)*—*(1c)* [R: see Table 1] leads to liberation of two moles of nitrogen and formation of the isocyanides *(3a)*—*(3c)* or the corresponding *N*-substituted formamides. The pentaazafulvenes *(2)* presumed to be formed as intermediates could neither be detected, even at −20 °C, nor trapped with *N*-phenylmaleimide or acetylenedicarboxylates. Oxidation with sodium hypobromite in aqueous medium and with lead tetraacetate/triethylamine in dichloromethane proved to be preparatively useful, while bromine/triethylamine and anodic oxidation[6] are less promising.

As an alternative to the oxidative degradation of *(1)* we attempted the elimination of sodium toluenesulfinate from the salt *(4a)*, which is formed by tosylation of *(1a)* in sodium hydroxide. *(4a)* was found to be unexpectedly stable; it starts

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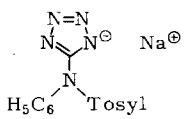
Table 1. Prepared isocyanides *(3)*. All compounds are spectroscopically pure and were isolated by distillation.

R	Yield [%] [a] on using NaOBr [b]	$Pb(OAc)_4$/NEt_3 [c] as oxidizing agent	Br_2/NEt_3 [c]	Anodic oxidation [b]
(3a) C_6H_5	92	70	43	39
(3b) n-C_4H_9	75			
(3c) C_6H_5—CH_2	84			48

[a] Yields can be improved.
[b] In 2 N sodium hydroxide solution.
[c] In dichloromethane.

to decompose at 280 °C, whereby, in addition to other unidentified products only small amounts of isocyanide are formed. Irradiation in aqueous solution led to the same result.



(4a)

Phenyl isocyanide (3a)

A solution of lead tetraacetate (2.7 g, 6.1 mmol) in dichloromethane (50 ml) is added dropwise within 15 min at 20 °C to a stirred solution of 5-phenylaminotetrazole *(1a)*[5] (0.89 g, 5.5 mmol) and triethylamine (1.3 g, 12.9 mmol) in dichloromethane (20 ml). The theoretical quantity of nitrogen is liberated. The dark-colored reaction mixture is concentrated in a vacuum at room temperature and the isocyanide *(3a)* extracted with petroleum ether; yield after concentration and distillation in a bulb-tube: 0.40 g (70%), b.p. 70 °C/20 torr.

n-Butyl isocyanide (3b)

To a solution of *n*-butylaminotetrazole *(1b)*[4] (6.25 g, 44.3 mmol) in 2 N sodium hydroxide (50 ml) is added 50 ml dichloromethane and the mixture stirred during dropwise addition of sodium hypobromite solution (4.9 mmol) at 0 °C (*ca.* 15 min). The aqueous phase is then extracted several times with dichloromethane, the combined organic phases dried over $MgSO_4$, and the solvent removed by distillation through a 40-cm packed column. Distillation of the residue affords *(3b)* b.p. 119—120 °C, in 75% yield (2.77 g).

Benzyl isocyanide (3c)

To a solution of 5-benzylaminotetrazole *(1c)*[4] (1.22 g, 7 mmol) in 2 N sodium hydroxide (50 ml) is added 20 ml ether at 0 °C. The stirred mixture is electrolyzed for 4 h at 3.8 V and 0.55 A[6]. The aqueous phase is extracted serveral times with ether, the combined organic phases dried with $MgSO_4$ and concentrated *in vacuo*. Distillation of the residue in a bulb-tube affords *(3c)*, b.p. 100 °C/16 torr in 48° yield (0.39 g).

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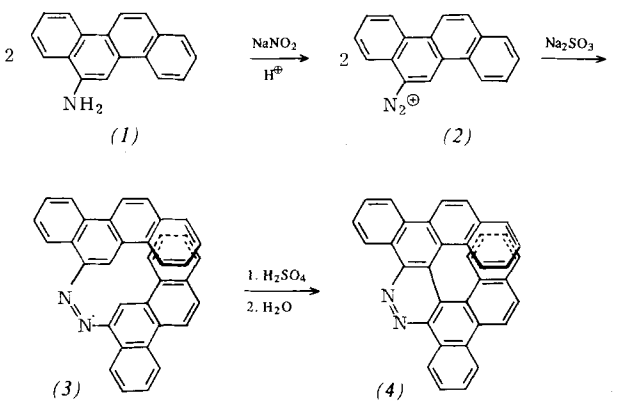
CAS Registry numbers:
(1a), 14832-59-8; *(1b)*, 57885-60-6; *(1c)*, 14832-58-7; *(3a)*, 931-54-4; *(3b)*, 2769-64-4; *(3c)*, 10340-91-7

[1] *G. Höfle*, Z. Naturforsch., in press.
[2] Known, *e.g.*, are the cleavage of α-iminolactones: *K. Bott*, Tetrahedron Lett. *1968*, 3323; *H. Kagen* and *I. Lillien*, J. Org. Chem. *31*, 3728 (1966); of iminocyclopropanes: *H. Quast* and *W. Risler*, Angew. Chem. *85*, 411 (1973); Angew. Chem. Int. Ed. Engl. *12*, 414 (1973) and of diaziridinimines: *H. Quast* and *E. Schmitt*, Angew. Chem. *81*, 428 (1969); Angew. Chem. Int. Ed. Engl. *8*, 448 (1969).
[3] *R. B. Woodward* and *R. Hoffmann*: The Conservation of Orbital Symmetry. Verlag Chemie, Weinheim 1970, pp. 152ff.
[4] *R. A. Henry* and *W. G. Finnegan*, J. Am. Chem. Soc. *76*, 926 (1954).
[5] *R. Stollé*, J. Prakt. Chem. *134*, 288 (1932); *W. L. Garbrecht* and *R. M. Herbst*, J. Org. Chem. *18*, 1278 (1953).
[6] Conditions: Carbon rod as anode, cylindrical copper cathode (length 3.5 cm), electrode gap 2 cm, 2 N sodium hydroxide without diaphragm.

Simple Synthesis and Resolution of a Diaza[7]helicene[**]

By *Hermann Rau* and *Otto Schuster*[*]

Diazahelicenes[1] containing a —N=N-grouping possess the structural elements of aromatic azo compounds. Since azo compounds behave spectroscopically and photochemically differently from the analogous carbon compounds on account of the longwave $n \rightarrow \pi^*$ transition[2], such diazahelicenes can be expected to display interesting properties.



We report here on a simple and very productive two-step synthesis of the diazadibenzo[7]helicene *(4)*[3] and on its resolution.

A suspension of 6-aminochrysene *(1)* (0.01 mol) in glacial acetic acid (20 ml) and conc. hydrochloric acid (7 ml) was diazotized to *(2)* with a solution of sodium nitrite (0.7 g) in water (3 ml). The cold solution was buffered with sodium acetate (3 g, anhydrous) in water (15 ml) and then treated dropwise with a saturated solution of sodium sulfite (1.55 g)[5] in water, whereupon 6,6'-azochrysene *(3)* precipitated out. After 10 minutes at 70 °C, *(3)* was filtered off, washed, and dried; yield 98%. A sample of the product, after recrystallization from toluene, was found to transform without melting at 268 °C into a yellow fluorescent solid which was not identical with the helicene *(4)*.—Crude *(3)* was dissolved in conc. sulfuric acid and precipitated almost quantitatively as helicene *(4)* on careful addition to water. After purification on a silica-gel-60 column with benzene, *(4)* was obtained as a yellow, strongly fluorescing substance of m.p. 345 °C.

The structure of *(4)* was confirmed by mass and CD spectra. The rapid quantitative transformation of *(3)* into *(4)* is surprising, for this would require that *(3)* be present only in the *cis* form.

The resolution of *(4)* was carried out with the π complexing agent TAPA, synthesized according to *Newman*'s method[6]. *(4)* and a threefold excess of (−)-TAPA were treated at 40 °C with just sufficient chloroform to dissolve them. After one day at 4 °C dark-red crystals of the complex of (−)-TAPA and an enantiomer of *(4)* had precipitated out. The crystals

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were dissolved in benzene and the solution subjected to chromatographic separation on a silica-gel-60 column with benzene.

Weight for weight, the ellipticities of the two enantiomer fractions were of the same magnitude but of different sign (±2%). This is indicative of complete separation, for otherwise equal values with opposite signs can occur only when the precipitated enantiomers and those remaining in solution each contain the same proportion of the other enantiomer[7]. The optical activity was not increased by a second resolution step.

In contrast to the analogous carbon compounds *(3)* is not cyclized to *(4)* in toluene/iodine with polarized light[8]. This is consistent with the photochemical behavior of azobenzene. A protonated form, which in the case of azobenzene can be photocyclized[9], is not formed—even in 70% perchloric acid.

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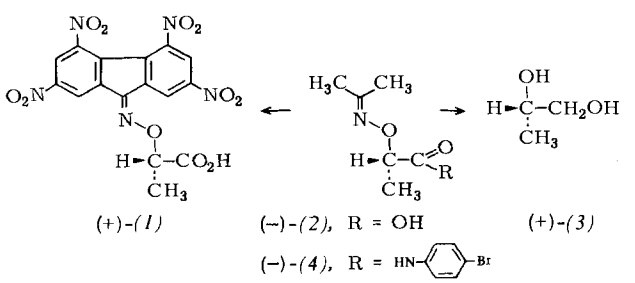
CAS Registry numbers:
(1), 2642-98-0; *(2)*, 57885-56-0; *(3)*, 57885-57-1; *(4)*, 57885-58-2

[1] *R. H. Martin*, Angew. Chem. *86*, 727 (1974); Angew. Chem. Int. Ed. Engl. *13*, 649 (1974).
[2] *H. Rau*, Angew. Chem. *85*, 248 (1973); Angew. Chem. Int. Ed. Engl. *12*, 224 (1973).
[3] Numerous attempts to prepare 6,6-azochrysene *(3)* by the usual methods [4], a) by oxidation of 6-aminochrysene, b) by reduction of 6-nitrochrysene, c) by condensation of 6-nitrochrysene with 6-aminochrysene, and d) by coupling of the diazonium salt *(2)* with chrysene, led to only insignificant yields of *(3)*.
[4] *K. H. Schündehütte* in Houben-Weyl: Methoden der Organischen Chemie. Thieme, Stuttgart 1965, Bd. 10/3, p. 213.
[5] *F. Suckfüll* and *H. Dittmer*, Chimia *15*, 137 (1961).
[6] *P. Block* and *M. S. Newman*, Org. Synth. *48*, 120 (1968).
[7] We thank Dr. *R. Lemke* for this information.
[8] *O. Buchardt*, Angew. Chem. *86*, 222 (1974); Angew. Chem. Int. Ed. Engl. *13*, 179 (1974).
[9] *G. E. Lewis*, J. Org. Chem. *25*, 2193 (1960).

Absolute Configuration of 2-(2,4,5,7-Tetranitro-9-fluorenylideneaminooxy)propionic Acid (TAPA)[**]

By *Thorsten Kemmer*, *William S. Sheldrick*, and *Hans Brockmann jr.*[*]

Since its use for the separation of enantiomers of hexahelicene[1, 2] 2-(2,4,5,7-tetranitro-9-fluorenylideneaminooxy)propionic acid (TAPA) *(1)* has proved to be a valuable reagent for the resolution of racemic Lewis bases, especially of those



(+)-*(1)* (−)-*(2)*, R = OH (+)-*(3)*
(−)-*(4)*, R = HN-C6H4-Br

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which contain no functional groups and therefore cannot be resolved by conventional methods.

Knowledge of the absolute configuration of *(1)* appeared essential if we were to improve our understanding of the interactions in the diastereomeric charge transfer complex.

To this end we have employed two independent methods: chemical correlation of *(1)* *via* 2-(isopropylideneaminooxy)-propionic acid *(2)* with 1,2-propanediol *(3)* and X-ray structure analysis of a derivative of *(2)*. The results obtained by the two approaches were in mutual agreement.

(−)-*(2)* can be converted into (+)-*(1)* by transoximation with 2,4,5,7-tetranitrofluorenone[1]. Reduction of *(2)* with $LiAlH_4$ in ether affords 1,2-propanediol *(3)*, which was transformed into the dibenzoate to facilitate characterization and purification. Subsequent hydrolysis of (−)-*(2)* ($[\alpha]_{578}^{22} = -34°$; $c = 1$, H_2O) gives *S*-(+)-*(3)*[3] ($[\alpha]_{578}^{22} = 8.2°$; $c = 0.17$; CH_3OH); (+)-*(2)* likewise leads to (−)-*(3)*[4]. Since no attack at the center of asymmetry is involved in this correlation the *S* configuration is therefore established for (+)-TAPA.

X-Ray structure analysis was performed on a crystal of (−)-2-(isopropylideneaminooxy)propion-*p*-bromoanilide *(4)* ($[\alpha]_D^{23} = -29°$; $c = 1$; benzene) which is readily accessible from (−)-*(2)* ($[\alpha]_D^{23} = -32°$; $c = 1$; H_2O) by aminolysis of the corresponding carboximidazolide[5] with *p*-bromoaniline. Compound *(4)* forms monoclinic crystals, $P2_1$, with $a = 12.979(5)$, $b = 10.411(6)$, $c = 10.138(4)$ Å; $\beta = 96.95(4)°$; $Z = 4$; $d_{calc.} = 1.46\,g\,cm^{-3}$. The structure was solved by Patterson and subsequent difference Fourier synthesis and refined to $R = 0.066$, $R_G = 0.082$ for 3242 independent reflections [Syntex $P2_1$, four-circle diffractometer, $(\Theta - 2\Theta)$ operation, $I \geq 2\sigma(I)$].

The methyl hydrogen atoms could not be unequivocally localized. The calculated positions of the other hydrogen atoms were included in the final cycles together with their associated isotropic temperature factors. The crystal lattice of *(4)* contains two mutually independent molecules which do not differ significantly with regard to their geometrical parameters; both exhibit the *S* configuration.

With the inverse coordinates $(-x, -y, -z)$ of the molecule (*i.e.* with those of the *R* form) the values of *R* and R_G deteriorate to 0.081 and 0.107 respectively. Thus the *S* configuration of (−)-*(4)*, and hence of (+)-*(1)*, is unequivocally proven.

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German version: Angew. Chem. *88*, 93 (1976)

[1] *M. S. Newman*, *W. B. Lutz*, and *D. Lednicer*, J. Am. Chem. Soc. 77, 3420 (1955).
[2] *M. S. Newman* and *D. Lednicer*, J. Am. Chem. Soc. *78*, 4765 (1956).
[3] *K. Freudenberg*: Stereochemie. Franz Deuticke Verlag, Leipzig 1933, p. 677; Beilstein, E III, *1*, 2158.
[4] The rotation of (−)-*(3)* was determined only qualitatively from the hydrolysis mixture of the dibenzoate.
[5] *H. A. Staab*, Angew. Chem. *74*, 407 (1962); Angew. Chem. Int. Ed. Engl. *1*, 351 (1962).

Cumulated Ylides as Building Blocks for the Synthesis of Heterocycles

By *Hans Jürgen Bestmann*, *Günter Schmid*, and *Dieter Sandmeier*[*]

Cumulated ylides *(1)*[1] react with compounds of type *(2)*, containing an acidic Y—H bond (Y = hetero atom) and a carbonyl function (Z = C—R) or a nitroso group (Z = N) in the same molecule, to give the heterocyclic compounds *(4)*.

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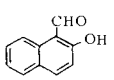
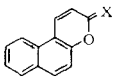
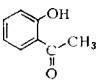
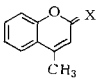
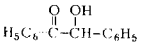
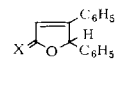
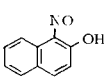
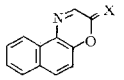
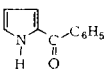
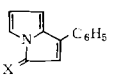
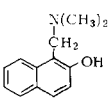
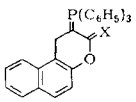
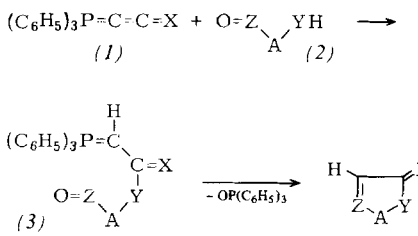
Table 1. Heterocyclic compounds *(4)* and *(7)* from cumulated ylides *(1)* and molecules of general structure *(2)* and *(5)*.

(2)	*(4)*	X	M.p. [°C] *(4)*	Yield [%]
		O	117	73
		$N-C_6H_5$	137	68
		$C_{13}H_8$ [a]	197	41
		$C_{13}H_8$ [a]	162	78
		O	149	58
		$N-C_6H_5$	209	29
		$N-C_6H_5$	183	71
		O	81	86
		$N-C_6H_5$	99	81

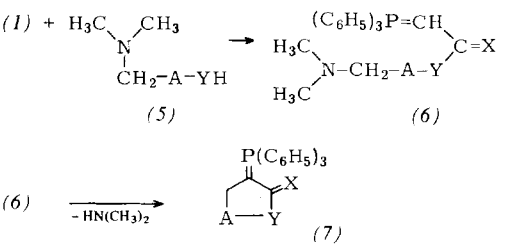
(5)	*(7)*	X	M.p. [°C] *(7)*	Yield [%]
		O	217	69
		S	172 [b]	93

[a] $C_{13}H_8$ = 9-fluorenylidene. [b] Softening begins without definite melting point.

The initial step of the reaction is addition of *(2)* to *(1)* to give *(3)*, from which *(4)* is formed by intramolecular Wittig reaction (Table 1).



The Z=O moiety in *(2)* can also be replaced by a Mannich base grouping $-CH_2-N-(CH_3)_2$. The intermediary product *(6)* formed from the resulting molecule *(5)* cyclizes with elimination of dimethylamine to give the ylide *(7)*, which can be employed in a number of further reactions[2] (Table 1).



Correct elemental analyses and spectroscopic data exist for all compounds *(4)* and *(7)* listed in Table 1.

Heterocycles (4)

(2) (10 mmol) is added slowly to a stirred solution of *(1)* (10 mmol) in anhydrous benzene (30 ml). The mixture is allowed to stand for 2—3 days or heated under reflux for *ca.* 24 h. After removal of solvent the residue is treated with hot methanol or isopropanol, filtered, and the filtrate transferred to a refrigerator. Compound *(4)* crystallizes out and can be purified by recrystallization from isopropanol or benzene/methanol.

Phosphoranes (7)

A stirred solution of *(1)* (10 mmol) and *(5)* (10 mmol) in anhydrous benzene (50 ml) is heated under reflux in an apparatus through which a slow stream of N_2 is allowed to pass. When evolution of dimethylamine is complete the reaction mixture is stirred for a further hour before removal of the solvent in a vacuum and recrystallization of the residue from ethyl acetate or benzene/ethyl acetate.

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revised: November 20, 1975
German version: Angew. Chem. *88*, 92 (1976)

[1] For new methods for synthesizing compounds *(1)* cf. *H. J. Bestmann* and *G. Schmid*, Angew. Chem. *86*, 479 (1974); Angew. Chem. Int. Ed. Engl. *13*, 473 (1974); *H. J. Bestmann* and *D. Sandmeier*, Angew. Chem. *87*, 630 (1975); Angew. Chem. Int. Ed. Engl. *14*, 634 (1975).

[2] Reviews: *H. J. Bestmann*, Angew. Chem. *77*, 609, 651, 850 (1965); Angew. Chem. Int. Ed. Engl. *4*, 585, 645, 830 (1965); *H. J. Bestmann* and *R. Zimmermann*, Fortschr. Chemischen Forsch. *20*, 1 (1971).

Synthesis of the 2*H*-1-Thiacyclobutabenzene System[**]

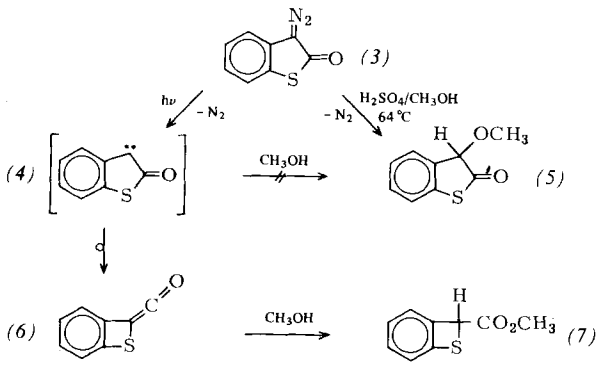
By *Erika Voigt* and *Herbert Meier*[*]

Thiete *(1)* and its simple derivatives are labile compounds at room temperature and tend to polymerize[1]. Their 1,1-dioxides *(2)*[2] are considerably more stable and better to handle. Stabilization is also possible by incorporation of the double bond of the system in an annelated benzene ring.

(1) *(2)*

We succeeded in synthesizing the first heterocycle of the type 2*H*-1-thiacyclobutabenzene (2*H*-1-benzothiete) by photolysis ($\lambda > 290$ nm) of the 3-diazo-2-oxo-2,3-dihydrobenzo[*b*]-thiophene *(3)*.

The photochemical primary step affords the carbene *(4)*, which subsequently rearranges to the ketene *(6)*. Addition of methanol to *(6)* leads to the methyl 2*H*-1-benzothiete-2-carboxylate *(7)* (b.p. 73 °C/0.06 torr, yield 30%). An alternative reaction which *(4)* might undergo is insertion into the O—H bond of the methanol with formation of the 3-methoxy-2-oxo-2,3-dihydrobenzo[*b*]thiophene *(5)*[3]. For confirmation of the structure of *(7)* we have prepared *(5)*, m.p. 50 °C, in 40% yield *via* an independent route by acid-catalyzed decomposition of *(3)*.

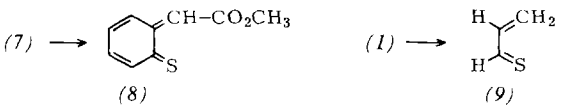


In contrast to the corresponding aza compounds *(5)* cannot be obtained by photolysis of *(3)*[4].

For the spectroscopic characterization of *(7)* a comparison with *(5)* and *(3)* is useful. The CO stretching vibration in the IR spectrum of *(3)* appears—as is usual for α-diazo carbonyl compounds—at low wave numbers (in KBr: 1640 cm^{-1}). In the thiolactone *(5)* the absorption is shifted to 1705 cm^{-1}, and in *(7)* it reaches the normal value of 1740 cm^{-1} for saturated aliphatic esters.

The ^{1}H-NMR spectrum of *(5)* recorded in $CDCl_3$ shows one singlet for the tertiary hydrogen at $\delta = 5.0$ ppm and one for the methyl protons at $\delta = 3.5$ ppm. In the case of the ester *(7)* both signals are shifted to lower field strengths (5.2 and 3.8 ppm, respectively). Especially informative are the ^{13}C-NMR spectra. The carbonyl carbon and the carbon atom adjacent to it give a marked high field shift of *ca.* 35 ppm on going from *(5)* through *(3)* to *(7)* ($\delta = 203.1$, 186.4 and 169.4 ppm, $\delta = 85.1$, 70.6, and 49.2, respectively; in $CDCl_3$, TMS internal)[5]. The resonance of the methyl C-atom in *(5)* lies at lower field strength than that of *(7)* ($\delta = 56.7$ and 52.8 ppm, respectively).

In contrast to *(3)* and *(5)* the bicyclic fundamental structural unit of *(7)* is considerably more stable towards fragmentation in the mass spectrometer.



(8) *(9)*

We attribute the greater thermal stability of *(7)* over *(1)* to the fact that the ring opening *(7)*→*(8)* is very much less energetically favorable than that of *(1)*→*(9)*.

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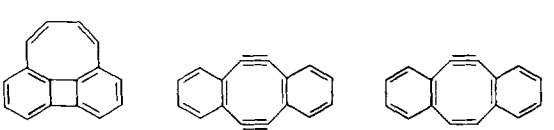
CAS Registry numbers:
(3), 54518-09-1; *(5)*, 58150-60-0; *(6)*, 58150-61-1; *(7)*, 58150-62-2; *(8)*, 58150-63-3; *(9)*, 53439-64-8

[1] *D. C. Dittmer, K. Takahashi*, and *F. A. Davis*, Tetrahedron Lett. *1967*, 4061.
[2] *D. C. Dittmer* and *M. E. Christy*, J. Org. Chem. *26*, 1324 (1961).
[3] Cf. also *H. Meier* and *K.-P. Zeller*, Angew. Chem. *87*, 52 (1975); Angew. Chem. Int. Ed. Engl. *14*, 32 (1975).
[4] *E. Voigt* and *H. Meier*, Angew. Chem. *87*, 109 (1975); Angew. Chem. Int. Ed. Engl. *14*, 103 (1975); Chem. Ber. *108*, 3326 (1975).
[5] For the ^{13}C-NMR of 1,2-dihydrocyclobutabenzene cf. *H. Günther, G. Jikeli, H. Schmickler*, and *J. Prestien*, Angew. Chem. *85*, 826 (1973); Angew. Chem. Int. Ed. Engl. *12*, 760 (1973); *W. Adcock, B. D. Gupta, T. C. Khor, D. Doddrell, D. Jordan*, and *W. Kitching*, J. Am. Chem. Soc. *96*, 1595 (1974).

5,6,9,10-Tetradehydrobenzocyclooctene, the Simplest Known Planar Neutral Conjugated Eight-Membered Carbocycle[1]

By *Henry N. C. Wong* and *Franz Sondheimer*[*]

The only known systems containing presumably planar neutral conjugated eight-membered rings are the dibenzoannelated compounds *(1)*[2], *(2)*[1, 3], and *(3)*[1]. As expected, the eight-membered rings in these substances prove to be paratropic ("antiaromatic"). It was desirable to make available simpler derivatives of these interesting systems. We now describe the synthesis of the very unstable 5,6,9,10-tetradehydrobenzocyclooctene ("benzo-1,5-cyclooctadiene-3,7-diyne") *(5)*, the simplest member yet isolated[4].



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

5,10-Dibromobenzocyclooctene ("3,8-dibromobenzocyclooctatetraene") *(4)* was prepared in *ca.* 10% overall yield by the photoinduced bromination of biphenylene in carbon tetrachloride (500 Watt clear lamp) for 30 minutes, followed by treatment of the resulting mixture of tetra- and hexabromocompounds[6] with an excess of sodium iodide in dimethylformamide at 50 °C for 4 hours[7]. The dibromide *(4)* in tetrahydrofuran was dehydrobrominated by addition to a stirred solution of potassium *tert*-butoxide (6 molar equivalents) in tetra-

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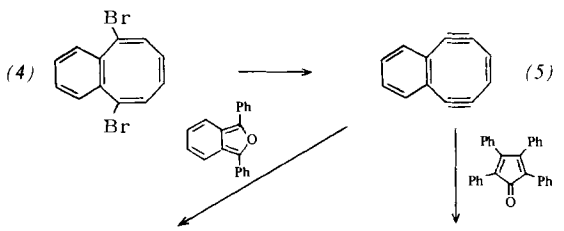
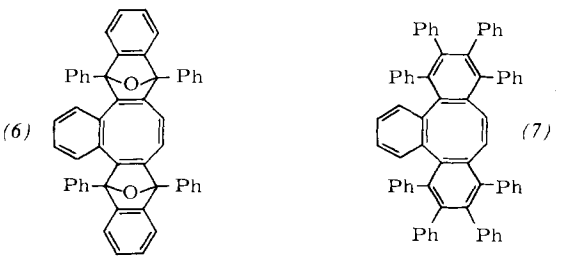
[**] The award (to H. N. C. W.) of a Shell Postgraduate Scholarship, administered by the Chinese University of Hong Kong, is gratefully acknowledged.

hydrofuran during 30 seconds at room temperature. Successive addition of 2 N hydrochloric acid, extraction with ether, drying, evaporation under reduced pressure at 0 °C, chromatography on alumina (Woelm, neutral, act. III) and elution with pentane yielded the diacetylene *(5)*. The isolation and chromatography procedure must be carried out as rapidly as possible (usually *ca.* 15 minutes) in view of the instability of *(5)*.

(5) is a yellow oil, which decomposes within a few minutes at 0 °C. It is also quite unstable in solution; this caused difficulties in estimating the yield and fully characterizing the substance (*e.g.*, no mass spectrum or satisfactory elemental analysis could be obtained). The charakteristic electronic spectrum of *(5)* in pentane showed maxima at 228 (ε = 23700), 233 (23300), 238sh (27000), 244 (46600), 249 (40700), 257 (71900), 327 (580), 332 (590), 341 (750), 345 (820), 361 (890), and 366 sh nm (750)[8]. The IR spectrum (CCl_4) exhibited a weak C≡C stretching band at *ca.* 2100 cm^{-1}. The ^{1}H-NMR spectrum ($CDCl_3$, 100 MHz, −20 °C) showed a sharp olefinic singlet at τ = 5.07 (which gradually disappeared on standing), but the exact location of the benzenoid multiplet was obscured by the appearance of bands due to decomposition products.





The structure of *(5)* was confirmed by the similarity of its electronic spectrum to that of *(2)*[1], the hypsochromic shifts of the three main maxima being 12—14 nm. The presence of two strained acetylenes in *(5)* was confirmed by its ready reaction with dienes. Thus, treatment of freshly prepared *(5)* with an excess of 1,3-diphenylisobenzofuran in pentane/ether at room temperature gave the bis-adduct *(6)*[9] (apparently as a single isomer), as colorless crystals, m. p. 208—209 °C; *m/e* 690.252 (calcd. 690.255); λ_{max} (dioxane) 228 (ε = 18100), 240 (24500), 258 (9100), 265sh (8100), 272sh (5900), and 282sh nm (3200); ^{1}H-NMR (CCl_4, 60 MHz), τ = 2.00—2.30 (m, 8H), 2.40—2.70 (m, 12H). 2.75—3.05 (including a sharp band at τ = 2.98) (m, 14H).

Treatment of *(5)* with an excess of 2,3,4,5-tetraphenylcyclopentadienone in pentane/ether at 40 °C led to the previously described[5] substance *(7)*[9], presumably derived from the initial adduct by elimination of carbon monoxide. Compound *(7)* formed colorless crystals, m. p. 305—307 °C (m. p. 308—312 °C[5]).

The similarity of the electronic spectrum of *(5)* to that of the benzoanalog *(2)* provides evidence that the eight-membered ring in *(5)* is essentially planar, as found for *(2)*[3]. The high-field resonance of the olefinic protons in the ^{1}H-NMR spectrum of *(5)* indicates the paratropicity ("antiaromaticity") of the eight-membered ring, as expected of a planar 4*n* π-system.

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German version: Angew. Chem. *88*, 126 (1976)

CAS Registry numbers:
(4), 17757-54-9; *(5)*, 58150-58-6; *(6)*, 58150-59-7; *(7)*, 35502-50-2

[1] Unsaturated eight-membered ring compounds. Part 12.—Part 11: *H. N. C. Wong, P. J. Garratt*, and *F. Sondheimer*, J. Am. Chem. Soc. *96*, 5604 (1974).
[2] *C. F. Wilcox, J. P. Uetrecht*, and *K. G. Grohmann*, J. Am. Chem. Soc. *94*, 2532 (1972); *C. F. Wilcox, J. P. Uetrecht, G. D. Grantham*, and *K. G. Grohmann, ibid. 97*, 1914 (1975).
[3] *R. Destro, T. Pilati*, and *M. Simonetta*, J. Am. Chem. Soc. 97, 658 (1975).
[4] Although substance *(5)* has not been isolated previously, it may have been an intermediate in the dehydrobromination of *(4)* with potassium *tert*-butoxide in the presence of 2,3,4,5-tetraphenylcyclopentadienone to give *(7)*[5].
[5] *J. W. Barton, T. A. Chaudri, P. Gaskin*, and *K. E. Whitaker*, J. Chem. Soc. Perkin Trans. I *1972*, 717.
[6] Separated from other products by chromatography on Merck Kieselgel $PF_{254+366}$.
[7] See *J. W. Barton, D. E. Henn, K. A. McLaughlan*, and *J. F. W. McOmie*, J. Chem. Soc. *1964*, 1622. We could not reproduce the direct formation of *(4)* in 25% yield by the photoinduced bromination of biphenylene in acetic anhydride (*J. W. Barton* and *K. E. Whitaker*, J. Chem. Soc. *C 1968*, 28).
[8] The ε values are minimum ones, due to the instability of *(5)*.
[9] Isolated by chromatography on Merck Kieselgel 60 PF_{254}.

$[W_3O_4F_9]^{5-}$: A Complex Ion of Tungsten(IV) Containing a W_3 Group

By *Karl Mennemann* and *Rainer Mattes*[*]

We have now been able to obtain the first oxofluoro anion of tungsten(IV): The ammonium salt $(NH_4)_5[W_3O_4F_9]\cdot 3H_2O$ is formed when a solution of the tungsten(V) compound $(NH_4)_2[W_2O_4(C_2O_4)_2(H_2O)_2]\cdot 0.5(NH_4)_2(C_2O_4)H_2O$[1] in 40% HF is heated to 70 °C and subsequently neutralized with $(NH_4)_2CO_3$. Under these conditions W^V disproportionates to W^{IV} and W^{VI}.

The anion $[W_3O_4F_9]^{5-}$ is diamagnetic and displays a hitherto unknown central atom to ligand ratio of 3:13. Surprisingly, it does not contain terminal oxygen atoms. In the IR spectrum (800—1000 cm^{-1}) the corresponding bands are absent. The intense bands at 780, 740, and 700 cm^{-1} are assigned to the stretching vibrations of the bridging oxygen atoms. The W—F stretching vibrations appear between 530 and 460 cm^{-1}. As shown by X-ray structure analysis[3] (cf. Fig. 1), the complex ion $[W_3O_4F_9]^{5-}$ is trinuclear; it has approximate C_{3v} symmetry and contains a cyclic W_3 group.

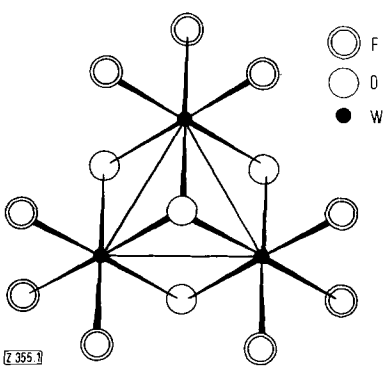

Fig. 1. Structure of the complex anion in $(NH_4)_5[W_3O_4F_9]\cdot 3H_2O$.

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The tungsten-tungsten bond length of 251.5(1) pm and magnetic behavior are consistent with the presence of W—W single bonds [cf. WO_2: d(WW) = 249 pm (double bond)[4]; $W_2Cl_9^{3-}$: d(WW) = 241 pm (triple bond)[5]].

Disregarding the metal atoms, each tungsten atom is surrounded by a distorted octahedron of three terminally bound fluorine atoms and three bridging oxygen atoms [d(WF): six bonds with lengths between 196(2) and 204(2) pm, mean value 201 pm, and three bonds each *trans* to the μ_3 oxygen and each with a length of 207(2) pm. Three of the four oxygen atoms lie 121 pm below [d(WO): 191(2) to 199(2) pm, mean value 195 pm] and the fourth (μ_3-O) 148 pm above the W_3 plane [d(WO): 207(2) pm, $\sphericalangle$WOW 74.9(1)°]. Similar structural units are to be seen in the three-dimensional crosslinked structures of Nb_3Cl_8[6] and $Zn_2Mo_3O_8$[7].

$[W_3O_4F_9]^{5-}$ represents the first example of an oxofluoro anion of a transition element not bearing terminally bound oxygen atoms. In the case of oxofluoro compounds with a central atom having d^0 configuration oxygen favors the terminal positions, since the effective charge of the central atom can be reduced by the formation of M—O π bonds. The polynuclear oxofluoro anions of Mo^{V}[8] and W^{V}[9] contain bridging oxygen atoms along with terminal ones. In $[W_3O_4F_9]^{5-}$ the formation of M—O π bonds does not take place because of the still lower oxidation state of the central atom.

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CAS Registry number:
$(NH_4)_5[W_3O_4F_9]\cdot 3H_2O$, 57789-33-0

[1] We suggest this formula for the compound first prepared by *Collenberg* [2] and hitherto formulated either as $(NH_4)_3[WO_2(C_2O_4)_2]\cdot 2H_2O$ or as $NH_4[WO_2(C_2O_4)]\cdot 2H_2O$.

[2] *O. Collenberg*, Z. Anorg. Allg. Chem. *102*, 247 (1918).
[3] Pailred data; 2087 reflections; $R = 0.073$.
[4] *A. Magneli, G. Anderson, B. Blomberg*, and *L. Kihlborg*, Anal. Chem. *24*, 1998 (1952).
[5] *W. Watson jr.* and *J. Waser*, Acta Crystallogr. *11*, 689 (1958).
[6] *H. Schäfer* and *H. G. von Schnering*, Angew. Chem. *76*, 833 (1964).
[7] *W. H. McCarrol, L. Katz*, and *R. Ward*, J. Am. Chem. Soc. *79*, 5410 (1957).
[8] *G. Lux* and *R. Mattes*, Angew. Chem. *86*, 598 (1974); Angew. Chem. Int. Ed. Engl. *13*, 600 (1974); Z. Anorg. Allg. Chem., in press.
[9] *K. Mennemann* and *R. Mattes*, unpublished work.

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

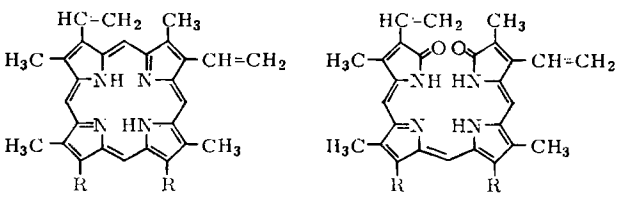
Synthetic amorphous calcium phosphate and its relation to the mineral matter of bones is the subject of a review by *A. S. Posner* and *F. Betts*. Inorganic constituents of bones are primarily calcium phosphate having the same Ca : P ratio as in hydroxyapatite $[Ca_{10}(PO_4)_6(OH)_2]$ and CO_3^{2-}, alongside traces of citrate and metal ions. The extremely small size of the crystals in bone material (200—300 Å) precludes X-ray studies on single crystals. Model studies showed that precipitation of hydroxyapatite from strongly supersaturated solutions always yields amorphous calcium phosphate initially which transforms autocatalytically to hydroxyapatite but can also be stabilized. Amorphous calcium phosphate obtained in this way, extremely finely divided synthetic hydroxyapatite, and mineral bone material were compared by X-ray diffraction techniques. Accordingly, the mineral bone material of adults probably consists predominantly of carbonate-containing hydroxyapatite whose structure is characterized by dislocations. [Synthetic Amorphous Calcium Phosphate and Its Relation to Bone Mineral Structure. Acc. Chem. Res. *8*, 273—281 (1975); 42 references]

[Rd 816—L IE]

The electron as a chemical entity is dealt with by *F. S. Dainton* in the "Faraday Lecture". Introductory theoretical considerations of the electron in condensed systems is followed by a discussion of how this species can be generated and how its most important physical and chemical properties have been elucidated. Knowledge about the solvated electron contributes, *inter alia*, to a better understanding of industrially important processes such as the hydrodimerization of acrylic compounds (*e.g.* acrylonitrile → hexanedinitrile) or the coupling of pyridine to give bipyridyl. [The Electron as a Chemical Entity. Chem. Soc. Rev. *4*, 323—362 (1975); 58 references]

[Rd 819 IE—F]

Bile pigments are summarized in an article by *M. F. Hudson* and *K. M. Smith*. Bile pigments are formed in nature by oxidative degradation of the prosthetic groups of hemopro-



(1) R = CH_2CH_2COOH *(2)*

teins. One example is the ring opening of the iron complex of protoporphyrin IX *(1)* to give biliverdin IXα *(2)* which in mammals undergoes further rearrangement. In mammals bile pigments are only waste products, whereas in lower animals they are often of vital importance, *e.g.* as pigments for protective coloring and as components of defense secretions; protein-bound bile pigments are photosynthetically active. [Bile Pigments. Chem. Soc. Rev. *4*, 363—399 (1975); 110 references]

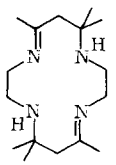
[Rd 820 IE—F]

Spin-lattice relaxation is designated by *L. D. Hall* in the "Tate and Lyle Lecture" as a fourth dimension for ^{1}H-NMR spectroscopy. In the ^{1}H-NMR spectra three types of parameters are usually evaluated: chemical shift, coupling constants, and areas under the signals. With newly developed instruments and techniques it has become possible to carry out routine measurements of spin-lattice relaxation times (T_1 values). The T_1 values reflect, *inter alia*, the spatial arrangement of the

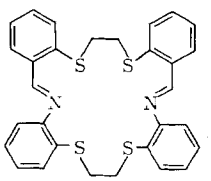
observed protons; the utility of this method is demonstrated using the investigation of carbohydrates as example. [Spin-Lattice Relaxation: A Fourth Dimension for Proton NMR Spectroscopy. Chem. Soc. Rev. *4*, 401—420 (1975); 33 references]

[Rd 821 IE—F]

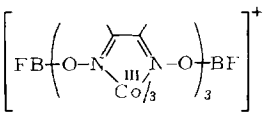
Transition metal complexes of synthetic macrocyclic ligands are discussed in an article by *L. F. Lindoy*. In addition to cyclic polyethers of the "crown" type, ring systems containing



(1)



(2)



(3)

nitrogen as donor, *e.g. (1)*, have also been investigated as ligands. Sulfur and phosphorus can also function as donor atoms. Crown compounds do not as a rule form stable complexes with transition metal ions, although ligands of type *(1)* do. Complete incorporation of a transition metal of the first series requires a 13 to 16-membered ring, in which the nitrogen atoms must be so arranged that five-, six-, or seven-membered rings are formed in the coordination of the metal ion. Ligands such as *(2)* having larger rings have to undergo twisting. *(3)* is an example of a three-dimensional "cage-like" complex. In addition to an outline of the synthesis and reactions of these compounds, models of biological macrocyclic systems such as vitamin B_{12} are also discussed. [Transition Metal Complexes of Synthetic Macrocyclic Ligands. Chem. Soc. Rev. *4*, 421—441 (1975); 95 references]

[Rd 822 IE—F]

Cyanides of metals from the 4th—7th subgroups are reviewed by *W. P. Griffith*. Though cyano complexes of all coordination numbers from eight to two are known, in the 4th—7th subgroups only octa-, hepta-, and hexacoordination have been established. The versatility of cyanide in the stabilization of oxidation states is exemplified by Mo and W (V to 0) and Re (VI to I). Methods of preparation are outlined, and metal-to-cyanide bonding is discussed. Transition metals with few d electrons will tend to use all five *n*d orbitals as well as $(n+1)$s and $(n+1)$p orbitals. The main part of the paper describes the chemistry of these complexes. [Cyanide Complexes of the Early Transition Metals (Group IVa—VIIa). Coord. Chem. Rev. *17*, 177—247 (1975); 359 references]

[Rd 823 IE—H]

BOOK REVIEWS

Methodicum Chimicum. General editor *F. Korte*. Vol. 6: C—N Compounds. Edited by *F. Zymalkowski*. Georg Thieme Verlag, Stuttgart and Academic Press, New York—London 1974. 1st Edit., viii, 864 pp., 104 tables, bound, DM 390.—.

The present volume[*] describes the methods used for the preparation of organic compounds containing nitrogenous groups. The chapters are arranged by compound classes, those treated being amines, carboxylic and thiocarboxylic acid derivatives containing nitrogenous groups, aliphatic diazo compounds*, organic *N*-oxides, hydrazines and hydrazones, aromatic diazonium salts*, oximes*, nitroso compounds, azido compounds*, amino carboxylic acids, azo and azoxy compounds, nitro compounds, hydroxylamines, nitriles, quaternary ammonium compounds, isocyanides/cyanates/thiocyanates, aziridines and azetidines, as well as aromatic hydrazo compounds. The chapters do not appear in the book in the same order as the above list but in the order of length, which varies from a maximum of 127 pages (for amines) to a minimum of 5 pages. There is no chapter on imines; moreover, rather unfortunately, the enamines are not treated separately but together with aliphatic and aromatic amines and are thus scattered.

The chapters are subdivided very rigidly according to the type of the preparative method (substitution, addition, redox reaction, condensation *etc.*); the range of application, the choice of reagents and reaction conditions, and the side reactions are discussed in detail. Particularly valuable are the tabulations, in some of which various processes are compared while in others examples are given of special methods and their yields. For experimental details the reader is directed to the original literature or to previous comprehensive publications, *e.g.* Houben-Weyl. The reactions of the various classes are described very briefly, if at all; only the chapters provided with an asterisk in the above list contain detailed descriptions of the possible reactions.

In spite of the large number (37) of authors who have contributed to this volume, the text is very uniform; there is hardly any overlapping, although Strecker synthesis appears in the chapters on amino carboxylic acids and on nitriles. This is due to the systematic approach, which occasionally degenerates into excessive formalism (Preface: "It was unavoidable that some methods of preparing organic nitrogen compounds could be treated either as N—N bonding or as rearrangements of other organo-nitrogen compounds"). Unfortunately this formal systematization is also the basis of the 56-page subject index, whose preparation must have been extremely laborious but which, in the reviewer's opinion, prevents rapid location of data not given in the clear contents list at the beginning of the book. Alongside a few general (and necessarily incomplete) headings such as "analysis" and named reactions, the index contains mainly individual compounds namely systematically according to Chemical Abstracts style and also groups of compounds ("amine/acetyl-alkyl"). In the last category, which is certainly very valuable for searches, the systematic approach is taken so far that, *e.g.* "enamines" contains only the statement "see under corresp. alkene"; in other cases the situation is not very clear: under "alkene/α-amino" we find two page numbers, one of which (p. 495) refers to the preparation of enamines from acetylenes and the other (p. 533) to that of allylamines from amides of α,β-unsaturated carboxylic acids; under "1-alkene/1-amino" we find only a

[*] Cf. Angew. Chem. *86*, 170 (1974); Angew. Chem. Int. Ed. Engl. *13*, 213 (1974).

single entry (p. 507), concerning the catalytic hydrogenation of aromatic nitro compounds containing "alk-1-en-1-yl substituents". It would be wise if the indexes of future volumes were constructed in a manner more adapted to their primary purpose.

In view of its comprehensive content and clear presentation this volume can be considered as an important reference work for problems of synthesis; for organic-chemical libraries it may be regarded as essential.

Günter Kresze [NB 294 IE]

Allgemeine und spezielle Pharmakologie und Toxicologie. (General and Specialized Pharmacology and Toxicology). Edited by *W. Forth, D. Henschler*, and *W. Rummel*. Wissenschaftsverlag, Bibliographisches Institut, Mannheim–Vienna–Zurich, 1975, 606 pp., numerous figures and tables, bound, DM 78.—.

In this book 25 authors set themselves the task of describing the material content of pharmacology and toxicology in relation to one another. Based on the subject list of the approbation law, the first part is devoted to general pharmacology and describes the interaction between drugs and living organisms. These principles make it easier to understand the appreciably larger second part concerned with the specialized pharmacology of organs and the possibilities available for treating them with drugs. Further chapters deal with the use of X-ray contrast media, the chemotherapy of infectious diseases, and the formation and treatment of tumors. An extensive section on poisons provides the conclusion.

The intention of this arrangement was to present in connected form material that is divided during studies between different departments. All the textual material concerned with pharmacotherapy is picked out in red. In this way the beginner who does not yet understand the principles merely has to turn the pages, while the more knowledgeable reader has in front of him all that belongs together. The large number of illustrations, usually in two colors, makes the text very easy to interpret, while numerous formulas in modern formulation and excellently drawn provide an easy overall view of the subject.

The reviewer, who is not a medical man, finds the underlying idea very good indeed. The pharmacological aspects are described with didactic skill and are easy for the general scientist to understand. Unfortunately, the information content of the individual chapters is very varied, as can be shown by comparing the section on endocrine pharmacology with the neighboring section on vitamins: in the former there are clear schematic illustrations of the mechanisms of action and regulation, and clear and detailed formulas for the biogenesis and metabolism of hormones; in contrast, for vitamins only brief indications are given in the text.

Apart from the section on vitamins, the sections on antimycotics, antiprotozoal drugs, and anthelmintics are underdeveloped from the point of view of the pharmaceutical chemist, as they are treated in a total of barely three pages and, after all, hundreds of millions of people suffer continuously from malaria, bilharzia, or hookworm.

Thus, although the scheme of the book is so illuminating, it could be greatly improved by thorough revision, which should not only root out the numerous printing errors and many wrong formulas but also remove factual errors; for example, phenazone is very readily soluble in water, chloral hydrate is not a chlorinated alcohol, tubocurarine is monoquaternary, colchicine is not the same as demecolcine, and if carboxylesterases really hydrolyze amides such as phenacetin or salicylamide this should be explained in more detail for the benefit of the uninitiated.

Thus, the Forth-Henschler-Rummel book in its present form is an attractively produced and impressive source of information; after thorough revision it would become a first-class textbook that would probably be in great demand.

Felix Zymalkowski [NB 296 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Terpenoids and Steroids, Vol. 5. Senior Reporter: *K. H. Overton*. The Chemical Society, London 1975. x, 390 pp., bound, £ 21.00.—A volume in the series "Specialist Periodica Reports".

Chemical Analysis of Organometallic Compounds, Vol. 4. By *T. R. Crompton*. Number 4 of the series "The Analysis of Organic Materials". Edited by *R. Belcher* and *D. M. W. Anderson*. Academic Press, New York 1975. x, 302 pp., bound, $ 23.25.

Chemisorption and Magnetization. By *P. L. Selwood*. Academic Press, New York 1975. ix, 172 pp., bound, $ 19.50.

Topics in Current Chemistry—Fortschritte der chemischen Forschung. Vol. 58: New Theoretical Aspects. Edited by *F. L. Boschke*. Springer-Verlag, Berlin 1975. iv, 186 pp., bound, DM 58.—.

Advances in Quantum Chemistry, Vol. 9. Edited by *P.-O. Löwdin*. Academic Press, New York 1975. x, 304 pp., bound, $ 42.00.

Baustoffchemie. Eine Einführung für Bauingenieure und Architekten. By *H. Henning* and *D. Knöfel*. Kohl's Technischer Verlag, Frankfurt 1975. 183 pp., bound, DM 25.—.

Histochemie. Grundlagen und Methoden. By *J. Chayen, L. Bitensky*, and *R. G. Butcher*. Verlag Chemie, Weinheim 1975. xv, 228 pp., paper, DM 58.—.

Physical Organic Chemistry. The Fundamental Concepts. By *C. D. Ritchie*. Vol. 4 of the series "Studies in Organic Chemistry". Edited by *P. G. Gassman*. Marcel Dekker, New York 1975. vii, 283 pp., bound, $ 16.50.

Statistical Mechanics and its Chemical Applications. By *M. H. Everdell*. Academic Press, New York 1975. xxii, 305 pp., bound, $ 22.75.

The Elementary Language of Solid State Physics. By *M. H. B. Stiddard*. Academic Press, New York 1975. xii, 188 pp., bound, $ 14.00.

Chemotherapie von Tumoren. Biochemische Grundlagen. By *W. E. G. Müller*. Verlag Chemie, Weinheim 1975. 155 pp., paper, DM 44.—.

Theory of Orientation and Stereoselection. By *K. Fukui*. Vol. 2 of the series "Reactivity and Structure Concepts in Organic Chemistry". Edited by *K. Hafner, J.-M. Lehn, C.-W. Rees, P. v. R. Schleyer, B. M. Trost*, and *R. Zahradník*. Springer-Verlag, Berlin 1975. vii, 134 pp., bound, DM 44.—.

Physiological and Biochemical Aspects of Heavy Elements in Our Environment. Edited by *J. P. W. Houtman* and *C. J. A. van den Hamer*. Delft University Press, Delft 1975. x, 77 pp., paper, Dfl. 35.—.—Proceedings of the Symposium in Utrecht, May 9, 1974.

Flame Emission and Atomic Absorption Spectrometry. Edited by *J. A. Dean* and *Th. C. Rains*. Vol. 3: Elements and Matrices. Marcel Dekker, New York 1975. xii, 674 pp., bound, $ 49.50.

Halonium Ions. By *G. A. Olah*. From the series "Reactive Intermediates in Organic Chemistry". Edited by *G. A. Olah*. John Wiley & Sons, New York 1975. xiii, 190 pp., bound, $ 22.75.

Das Verpackungswesen im letzten Viertel des 20 Jahrhunderts. Ausgewählte Probleme der Verpackungswissenschaft, der Verpackungswirtschaft und der Verpackungsinstitutionen. Edited by *H. Prast*. Econ Verlag, Düsseldorf 1975. 555 pp., bound, DM 48.—

Crystal Growth from High-Temperature Solutions. By *D. Elwell* and *H. J. Scheel*. Academic Press, New York 1975. xi, 634 pp., bound, $ 52.25.

Structure and Bonding. Edited by *J. D. Dunitz, P. Hemmerich, R. H. Holm, J. A. Ibers, C. K. Jørgensen, J. B. Neilands, D. Reinen*, and *R. J. P. Williams*. Vol. 24: Photoelectron Spectrometry. Springer-Verlag, Berlin 1975. iv, 169 pp., bound, DM 68.—

Physical Chemistry Series Two, Vol. 1: Theoretical Chemistry. Edited by *A. D. Buckingham* and *C. A. Coulson*. From the series "International Review of Science". Butterworths, London 1975. xxvi, 396 pp., bound, £ 13.45.

Physical Chemistry Series Two, Vol. 4: Magnetic Resonance. Edited by *C. A. McDowell*. From the series "International Review of Science". Butterworths, London 1975. 239 pp., bound, £ 13.45.

Physical Chemistry Series Two, Vol. 8: Macromolecular Science. Edited by *C. E. H. Bawn*. From the series "International Review of Science". Butterworths, London 1975. 303 pp., bound, £ 13.45.

Mimc Microforms Annual 1976. Featuring Releases of Microforms International Marketing Company and 31 Other Major Micropublishers. Microforms International Marketing Company, A Division of Pergamon Press, Fairview Park 1975. 296 pp., paper.

The Organic Chemistry of Electrolyte Solutions. By *J. E. Gordon*. From the series "Interscience Monographs on Organic Chemistry". Edited by *G. A. Olah*. John Wiley & Sons, London 1975. xxi, 554 pp., bound, £ 15.35.

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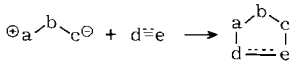
Intramolecular 1,3-Dipolar Cycloaddition Reactions

By Albert Padwa[*]

The intramolecular 1,3-dipolar cycloaddition reaction of suitably functionalized 1,3-dipoles represents a general scheme for the synthesis of novel fused ring heterocycles. Such reactions of a number of 1,3-dipoles are summarized and the general outline and potential analogies for these reactions noted. While the immediate aim of this review is to survey and correlate published work, it is hoped that general and specific points in need of study will be revealed and will stimulate further work in this fertile field.

1. Introduction

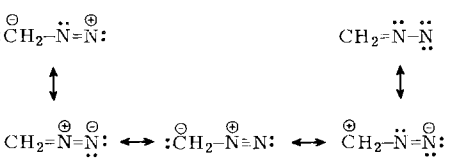
Huisgen et al. were the first to recognize fully the general concept and scope of 1,3-dipolar cycloadditions[1–5], a reaction of considerable scope for the synthesis of five-membered heterocyclic rings. 1,3-Dipolar cycloadditions are bimolecular in nature and involve the addition of a 1,3-dipole to a multiple bond system leading to five-membered heterocycles, according to Scheme 1.



Scheme 1

A 1,3-dipole is basically a system of three atoms over which are distributed four π electrons as in the allyl anion system. The three atoms can be a wide variety of combinations of C, O, and N. The dipolarophile can be virtually any double or triple bond. The term "1,3-dipole" arose because in valence bond theory such compounds can only be described in terms of dipolar resonance contributors, as shown for diazomethane.

The extreme 1,3-dipolar forms with their complementary nucleophilic and electrophilic centers readily explain the tendency to undergo addition to π bonds. Indeed, it must be possible to write 1,3-dipolar forms for all such species which undergo this type of addition.



Huisgen et al. have systematically studied the mechanism of 1,3-dipolar cycloadditions[1–3]. In the great majority of 1,3-cycloadditions, the reaction rate is not markedly influenced by the dielectric constant of the solvent medium in which the reaction is conducted. The independence of solvent polarity[6], the very negative entropies of activation[7], and the stereospecificity and regiospecificity[2] point to a highly ordered transition state. In most instances of 1,3-dipolar cycloaddition reactions, when two isomers are possible as a result of the use of unsymmetrical reagents, one isomer usually predominates, often to the exclusion of the other[8, 9].

The principal question that arises when considering the regiospecificity of 1,3-dipolar additions is whether the two new σ bonds formed on addition of the 1,3-dipole to the dipolarophile are formed simultaneously or one after the other. The mechanism that has emerged from *Huisgen*'s group is

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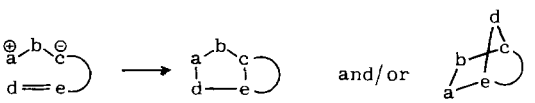
that of a single-step, four-center, "no-mechanism" cycloaddition, in which the two new bonds are both partially formed in the transition state, although not necessarily to the same extent[1-3]. A symmetry-energy correlation diagram reveals that such a thermal cycloaddition reaction is an allowed process[2, 10, 11]. An alternative mechanism that has been proposed is a two-step process involving a spin-paired diradical intermediate[12].

The regioselectivity of 1,3-dipolar cycloaddition reactions has, until recently, been a most difficult phenomenon to explain. Rationalizations of regioselectivity based on a concerted transition state model have invoked both electronic and steric effects[1-3, 13]. A solution to the vexing problem of regioselectivity in 1,3-dipolar cycloadditions has recently been proposed by *Houk et al.*[14-17], who used the frontier orbital method for rationalizing the effect of substituents on rates and regioselectivity of 1,3-dipolar cycloadditions. According to the frontier orbital treatment of 1,3-dipolar cycloadditions[14-18], the relative reactivity of a given 1,3-dipole toward a series of dipolarophiles will be determined primarily by the extent of stabilization afforded the transition state by interaction of the frontier orbitals of the two reactants. Reactions have been classified[18] into three types depending on whether the dominant interaction is between the highest occupied molecular orbital (HOMO) of the dipole and the lowest unoccupied molecular orbital (LUMO) of the dipolarophile, or the dipole LUMO and the dipolarophile HOMO, or whether both these interactions are of equal significance. The energies of both HOMOs are increased by the presence of electron-donating (including alkyl) and conjugating substituents and the energies of both LUMOs are decreased by electron-withdrawing and conjugating substituents[14-17].

This frontier orbital model also deals with the problem of regioselectivity of addition. In order to predict regioselectivity, it becomes necessary to determine the relative magnitudes of the coefficients in the HOMO and LUMO of the 1,3-dipole and dipolarophile. The favored cycloadduct will be that formed by union of the atoms with the largest coefficients. Further mechanistic discussion is to be found in the original literature.

In spite of the copious literature dealing with bimolecular 1,3-dipolar cycloaddition reactions, intramolecular examples have received only a minimum of attention. 1,3-Dipoles bearing a functional group able to behave as a dipolarophile are extremely interesting substrates. In fact, the intramolecular cycloaddition of a properly functionalized 1,3-dipole represents a general scheme for the synthesis of novel fused ring heterocycles (see Scheme 2).

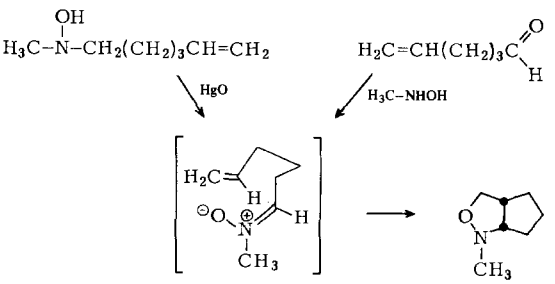


Scheme 2

In the present paper, the findings dealing with intramolecular 1,3-dipolar cycloadditions will be reviewed.

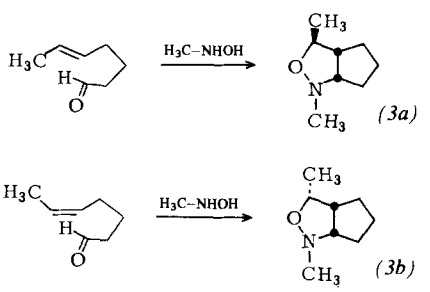
2. Nitrones

1,3-Dipolar cycloadditions of nitrones have been reported with a variety of alkynes, alkenes, isocyanates, isothiocyanates, thiocarbonyl compounds, phosphoranes, sulfenes, and sulfinyl groups[19]. All these reactions are usually carried out by heating the two reagents together in an inert solvent, and the products are often easily isolated in high yield. It should be pointed out that the cycloadducts are not stable in all cases and sometimes undergo interesting transformations. Whereas the cycloaddition of a simple alkene to a simple nitrone produces a simple isoxazolidine, a fused bicyclic isoxazolidine *(2)* can be formed when the alkene and nitrone moieties are suitably arranged in the same molecule. This useful synthetic idea was first investigated by *LeBel et al.*[20], using molecules in which the nitrone was separated by a propylene or butylene chain from the alkene. The unsaturated nitrone *(1)* was not isolated but was generated either by oxidation of an *N*-alkenylhydroxylamine or by condensation of an unsaturated aldehyde with *N*-methylhydroxylamine.



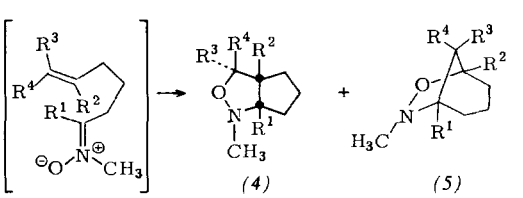
(1) *(2)*

When the cycloaddition was carried out with *trans*- and *cis*-5-heptenal, two different isoxazolidines, *(3a)* and *(3b)*, respectively, were obtained. It is apparent from these results that the intramolecular addition is kinetically controlled and that the configuration of the olefin is retained in the product isoxazolidine. Internal cycloaddition to give the *cis* fused bicyclo[3.3.0]octane skeleton is preferred since closure to the highly strained *trans* fused isomer would involve a transition state of much higher energy.



(3a) *(3b)*

A preference was found for the formation of the (fused) bicyclo[3.3.0]octane system *(4)*, but the (bridged) bicyclo[3.2.1]octane system *(5)* appeared when bond formation between the 2-position of the alkene and the α-position of the nitrone was hindered by substitution in those positions[21].

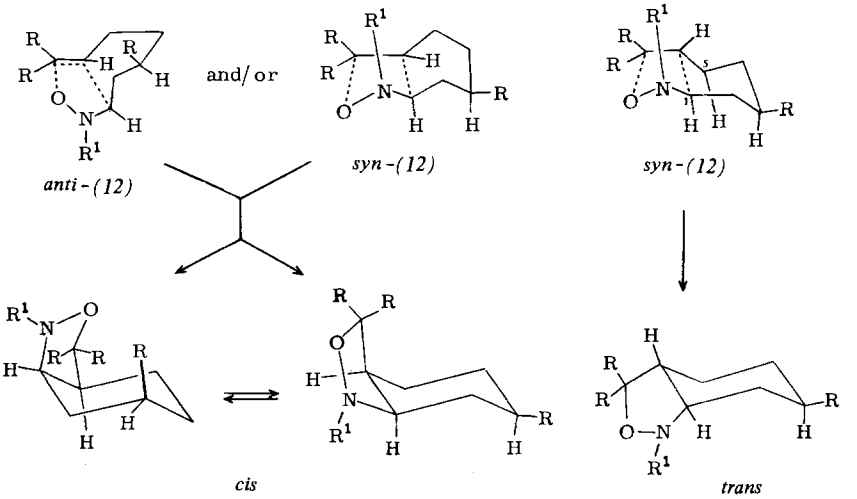


(4) *(5)*

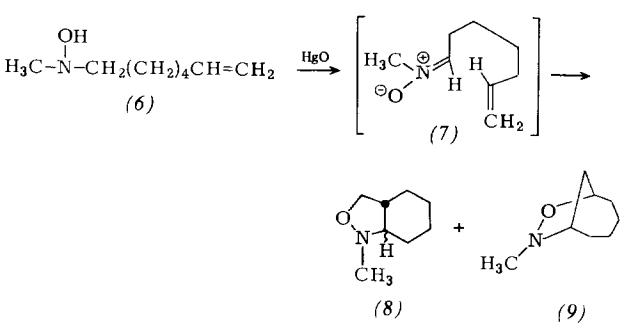
For example, when only one of the substituents R^1, R^2, R^3, and R^4 is a methyl group and the others hydrogen atoms, only the fused product *(4)* is formed, but when $R^1=R^2=CH_3$

and $R^3=R^4=H$ approximately equal amounts of fused *(4)* and bridged *(5)* products are formed. The presence of methyl groups in these positions (*i.e.* $R^1=R^2=CH_3$) forces them to be strongly eclipsed in the transition state leading to the normal fused product *(4)*. In this case, the severe steric interactions allow for the competing formation of the bridged product *(5)*.

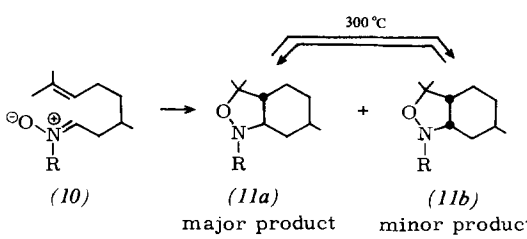
isoxazolidine into nitrone *(10)* followed by ring closure to give a product with the opposite stereochemistry. This isomerization represents an example of the reversibility of the intramolecular cycloaddition of an unsaturated nitrone. Retro 1,3-dipolar additions have been previously noted with intermolecular examples of nitrone-olefin adducts[24] and provides reasonable analogy for the above interconversion.



The cycloaddition reaction was extended to include the homologous nitrone *(7)*[22]. Mercuric oxide oxidation of *N*-6-heptenyl-*N*-methylhydroxylamine *(6)* afforded a mixture of *cis*- and *trans*-*N*-methyl-8-oxa-7-azabicyclo[4.3.0]nonane *(8)* (ratio 2:1) as well as lesser quantities of a product having the bicyclo[4.2.1]nonane structure *(9)*.



Under conditions of kinetic control, the *cis* ring fusion [cf. *(8)*] predominated in the condensation of 6-heptenal with methylhydroxylamine. However, the major product *(11a)* derived from (+)-citronellal and *N*-substituted hydroxylamines was shown to have the *trans* ring fusion. In this

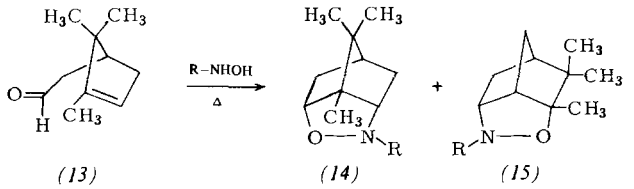


case the stereochemistry was found to be temperature dependent; increasing proportions of *(11b)* were obtained at high reaction temperatures[23]. At 300 °C the *trans* fused isoxazolidine *(11a)* undergoes partial isomerization to the *cis* isomer. This process was rationalized by thermal conversion of the

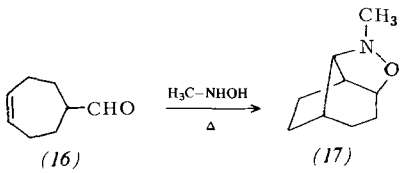
In order to rationalize the stereochemical results, *LeBel* suggested that the transition state leading to *cis* ring fusion requires the potential six-membered carbocyclic ring to adopt a twist conformation. A slightly deformed chair arrangement will produce the *trans*-isomer. Examination of models indicates that orbital overlap for 1,3-addition is favorable for a *cis* ring juncture for both *syn*- and *anti*-configurations of the intermediate nitrone *(12)*. Effective overlap in the transition state for formation of a *trans*-fused product is essentially precluded with an *anti* nitrone, and only the more favorable *syn* arrangement can lead to product. It is quite reasonable to assume that the ground state equilibrium composition of the nitrone favors the *anti* configuration. If the barrier to *syn*→*anti* isomerism is of the order of magnitude of the activation energies for intramolecular addition, then *cis* product will be favored. On the other hand, if the barrier to rotation in the nitrone is low, then the ratio of products will depend only on the difference in free energy levels of the respective transition states (Curtin-Hammett principle). In the transition state leading to *trans* isomer, a significant interaction develops between the 1-H and the 5-methylene group which allows the seemingly less favorable twist arrangement of the tetramethylene chain leading to *cis*-isomer to compete successfully. This would account for the observed isomer ratio of 2:1 (*cis*/*trans*) in the condensation of 6-heptenal with methylhydroxylamine. With citronellal, the *trans* product is more stable than the *cis* compound, and product development control predominates.

LeBel et al. further demonstrated the utility and synthetic scope of the intramolecular 1,3-dipolar cycloaddition of nitrones by preparing a variety of polycyclic isoxazolidines[21, 25–27]. Examples include the syntheses of compounds *(14)*, *(15)*, *(17)*, *(19)*, *(21)*, *(23)*, and *(25)*.

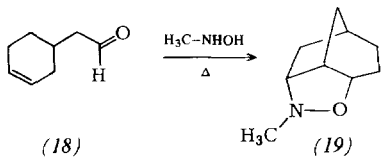
These ring closure reactions were suggested to be initiated by electrophilic attack of the nitrone on the olefin, the nitrone carbon atom thus resembling a carbenium ion center[25]. No



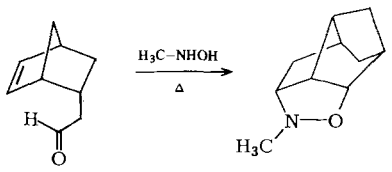
(13) (14) (15)



(16) (17)



(18) (19)



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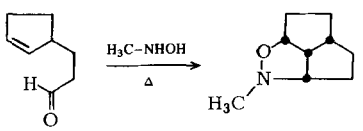

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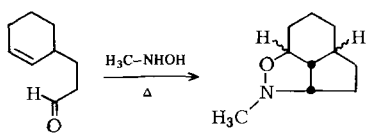
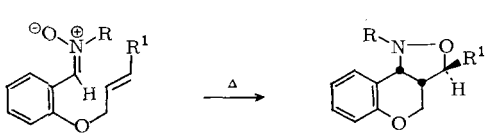


(24) (25)

distinction was made between a one-step process or a two-stage mechanism involving a rapid second step.

Oppolzer et al.[28-30] have extended the intramolecular 1,3-dipolar cycloaddition reaction to include nitrone-alkenes separated by chains that generally incorporate a benzene ring and a heteroatom to produce isoxazolidines *(27)* and *(29)*.

In most of the cases examined the isoxazolidine was found to contain a *cis*-ring junction between the heterorings. Adducts



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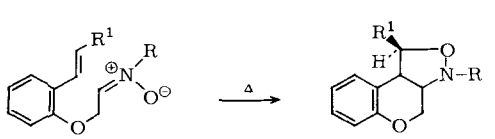
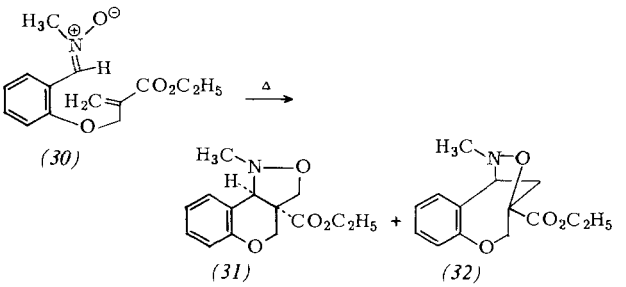
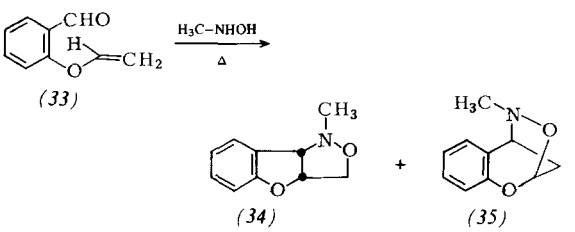


(28) (29)

with bridged structures such as *(32)* and *(35)* were also formed in some cases[28-30].

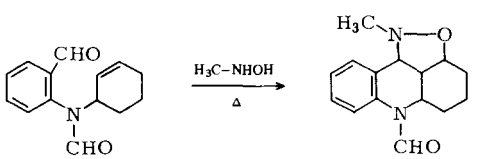


(30) (31) (32)



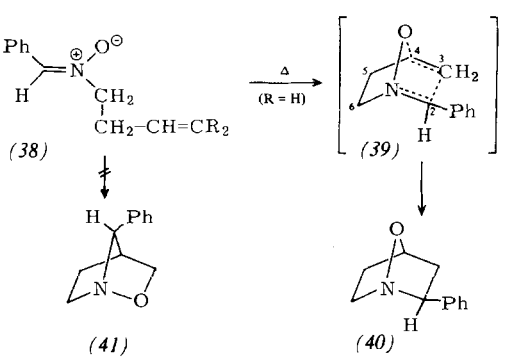
(33) (34) (35)

Also, the ether oxygen can be replaced by a formamido group which results in the formation of the related tetrahydroquinoline product *(37)*[28].



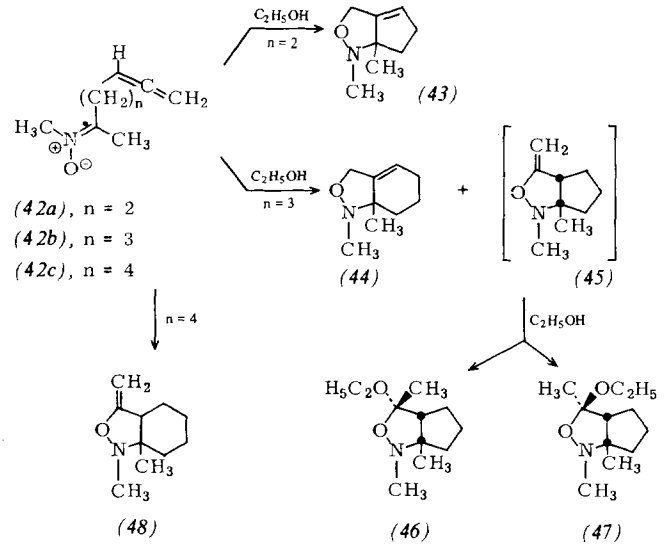
(36) (37)

When the alkene functionality is attached to the nitrone's nitrogen atom, only bridged structures are formed[31]. In the case of *N*-3-butenyl nitrone *(38)*, the terminal alkene carbon atom takes part in CC bond formation.



(38) (39) (41) (40)

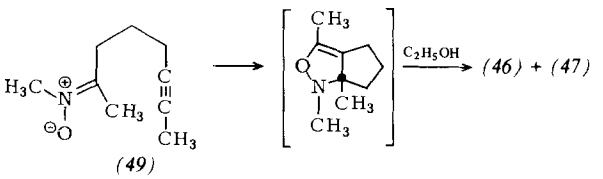
Cycloaddition fails for the *N*-butenyl system where R = CH_3, presumably owing to considerable steric hindrance in the transition state. The preferential formation of *(40)* rather than *(41)* has been attributed to steric destabilization of the transition state for the formation of the latter compound[31]. Inspection of Dreiding models of nitrone *(38)* reveals that significant σ overlap between O and C-4 and between C-2 and C-3 in transition state *(39)* cannot develop simultaneously unless the latter assumes product-like geometry[31]. The preference for *(40)* could also be explained by electronic factors. The formation of this isomer corresponds to the electronically favored addition direction of a nitrone to a monosubstituted ethylene[32].



(42a), n = 2
(42b), n = 3
(42c), n = 4

(43) (44) (45) (48) (46) (47)

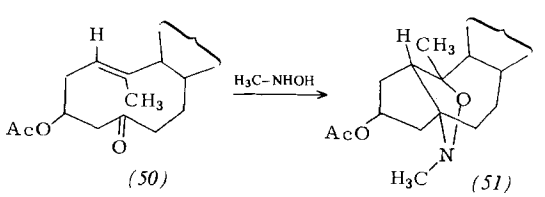
The intramolecular cyclization of allenic nitrones was found to afford several novel bicyclic products[33]. Treatment of 5,6-heptadien-2-one with *N*-methylhydroxylamine gave a transient nitrone *(42a)* which produced the unsaturated bicyclic isoxazolidine *(43)* by intramolecular cycloaddition at the terminal double bond of the allenic function. Cyclization of the homologous nitrone *(42b)* gave bicyclic adduct *(44)* as well as the stereoisomeric isoxazolidines *(46)* and *(47)*. The data indicate that the *exo*-methyleneisoxazolidine *(45)* is initially formed by addition of the nitrone to the internal bond of the allenic group. Subsequent acid catalyzed addition of ethanol produced the ethers *(46)* and *(47)*. A related set of reactions occurred with acetylenic nitrone *(49)*[33].



(49) (46) + (47)

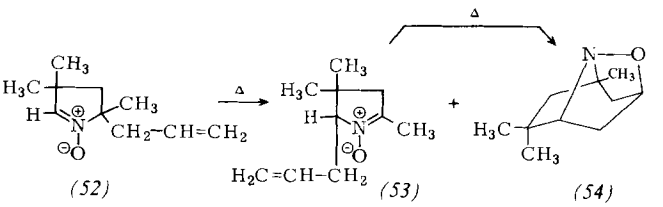
Treatment of 7,8-nonadien-2-one with *N*-methylhydroxylamine gave nitrone *(42c)* which cyclized to bicyclic adduct *(48)* by addition of the nitrone moiety to the internal carbon-carbon double bond of the allenic function. Thus the product formed in these intramolecular cyclizations depends on the separation of the allene and nitrone groups.

Reaction of the 1(10)-unsaturated *trans*-5-oxo-5,10-secosteroid *(50)* with *N*-methylhydroxylamine has been reported to give a non-isolable nitrone which undergoes spontaneous transannular cyclization with formation of the *N*-methylisoxazolidine derivative *(51)* in over 60% yield[34]. The geometry of the *trans*-cyclodecenone ring in the modified steroid compound is favorable for transannular 1,3-dipolar cycloaddition. In contrast, the diastereomeric 1(10)-unsaturated *cis* nitrone system does not undergo intramolecular 1,3-dipolar addition since the double bond between C-1 and C-10 and the trigonal C-5 atom of the *cis*-cyclodecenone ring are too far apart to permit the internal cyclization reaction to occur.



(50) (51)

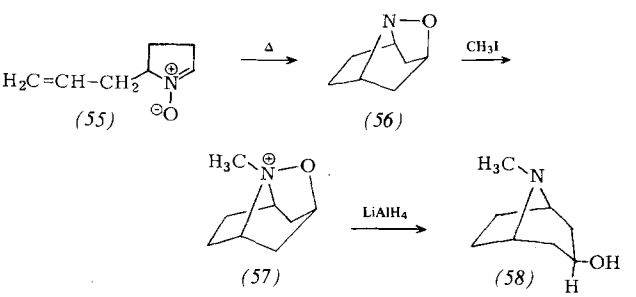
Bapat et al.[35] have recently described the thermal behavior of a cyclic nitrone, 5-allyl-3,3,5-trimethyl-1-pyrroline *N*-oxide *(52)*, which gives both a Cope rearrangement product *(53)* and an internal cycloaddition product *(54)* when heated in an inert solvent[35]. The proportions of the two rearranged products varied as a function of the thermal conditions used.



(52) (53) (54)

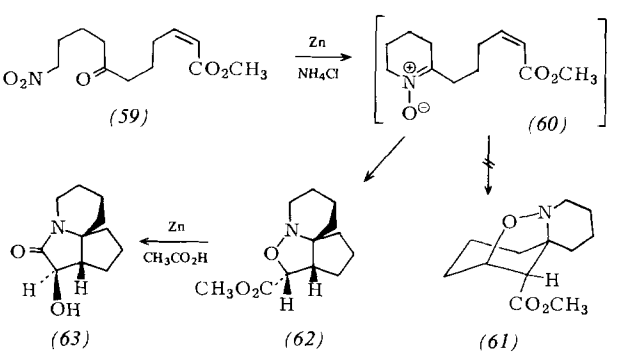
Heating nitrone *(52)* in boiling toluene for 1 h gave the Cope rearrangement product *(53)* as the only isolable product. The rearranged nitrone *(53)* was slowly converted into cycloadduct *(54)* in boiling xylene, and this cycloadduct could most conveniently be prepared by heating *(52)* in boiling xylene for 5 h. Thus the formation of cycloadduct *(54)* can be attributed to cyclization of the rearranged nitrone *(53)*.

The intramolecular dipolar addition of 5-allyl-1-pyrroline *N*-oxide *(55)* has been found to give a cycloadduct *(56)* which is a useful precursor of the tropane skeleton[36]. This conversion was achieved by methylation of *(56)* with methyl iodide to give the quarternary salt *(57)* which gives pseudotropine *(58)* upon reduction with lithium tetrahydridoaluminate.



(55) (56) (57) (58)

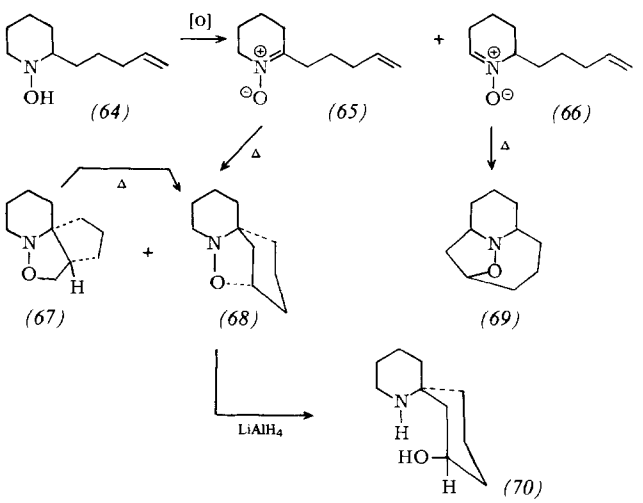
An elegant approach to the ring skeleton of histrionicotoxin involving an intramolecular cyclization of a nitrone moiety with an activated olefin has recently been attempted by two groups of workers[37, 38]. Cyclization of nitrone ester *(60)* was considered to offer high promise for producing the desired ring system *(61)* of histrionicotoxin. However, treatment of nitro-ketone *(59)* in aqueous methanol with zinc and ammonium chloride gave only cycloadduct *(62)* *via* spontaneous cyclization of a transient nitrone intermediate *(60)*. Chemical evidence for the structure of *(62)* was obtained



(59) (60) (63) (62) (61)

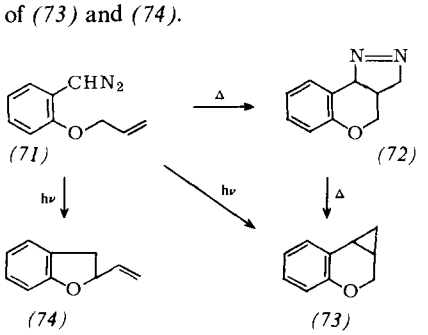
by cleavage of the nitrogen-oxygen bond with zinc and acetic acid to the hydroxy lactam *(63)*. The formation of *(62)* rather than *(61)* from the nitrone cyclization was attributed to the greater steric interactions in the transition state leading to *(61)*[37].

It is interesting to note that cyclization of the closely related unsaturated nitrone *(65)* resulted in the formation of both regioisomers *(67)* and *(68)*[38]. Nitrone *(65)* as well as smaller quantities of the isomeric nitrone *(66)* were generated by oxidation of the hydroxylamine derivative *(64)*. The major cycloadduct *(67)* was thermally isomerized to the thermodynamically more stable compound *(68)* having a bicyclo[3.2.1]octane partial structure, presumably by way of a 1,3-dipolar cycloreversion. Reduction of the nitrogen-oxygen bond of *(68)* afforded *cis*-1-azaspiro[5.5]undecan-8-ol *(70)* which contains the skeleton of histrionicotoxin (without side chains)[37, 38].

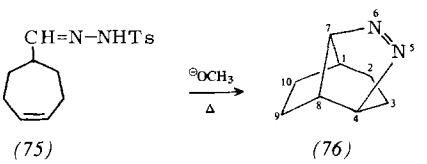


3. Diazoalkanes

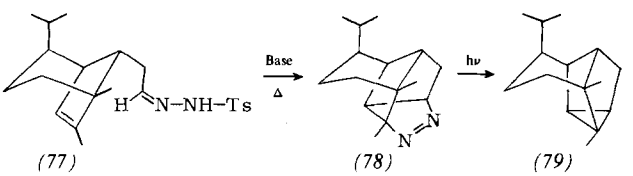
1,3-Dipolar cycloadditions of diazoalkanes to multiple bonds was first observed in 1888 by *Buchner*[39]. Since the initial report, many examples have appeared in the literature[1-5]. There are, however, only a few reports dealing with the intramolecular addition of diazoalkanes to carbon-carbon double bonds. *Kirmse* and *Dietrich* reported that the thermolysis of *(71)* gave 1-pyrazoline *(72)* in 80% yield[40]. On further heating, the initially formed 1-pyrazoline lost nitrogen to give the corresponding cyclopropane *(73)*. In contrast to the thermal results, photolysis of *(71)* produced a mixture of *(73)* and *(74)*.



The major product of the reaction of 4-cycloheptenecarbaldehyde tosylhydrazone *(75)* was found to be 5,6-diazatricyclo[5.3.0.0^{4,8}]dec-5-ene *(76)*[41]. This product was formed by intramolecular 1,3-cycloaddition of the diazomethane part of the molecule to the double bond. The authors noted that the double bond has a considerable activating influence on the decomposition of the tosylhydrazone anion and that the cycloaddition of the diazomethane moiety occurred much faster than the competing reaction of carbene formation. Normally pyrazoline formation with unactivated double bonds is a very sluggish reaction[1]. The significant lowering of the temperature at which the tosylhydrazone anion decomposed was attributed to double-bond participation[41].

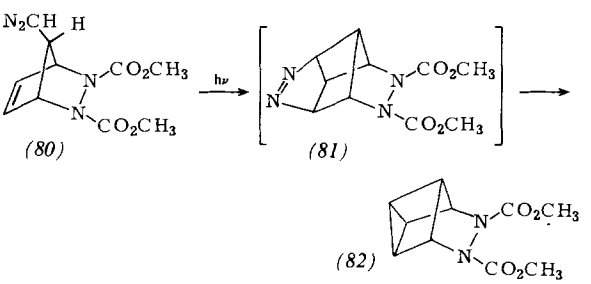


A similar internal cycloaddition occurred[42] when the lithium salt of tosylhydrazone *(77)* was heated at 120 °C. The cycloadduct obtained *(78)* (81 %) was converted into cyclocopacamphene *(79)* on further photolysis. The facile intramolecular 1,3-dipolar cycloaddition of the intermediate olefinic diazoalkane to give *(78)* is presumably related to the proximity



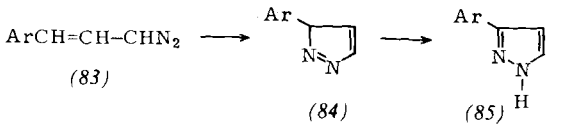
of the two reacting functional groups and to the fairly strained nature of the olefinic double bond.

Trost et al.[43, 44] have recently developed a simple approach to the 7,8-diazatetracyclo[3.3.0^{2,4}.0^{3,6}]oct-7-ene system *(82)*. Irradiation of diazo compound *(80)* generated the tetracyclic framework *(82)* in reasonable yield. The success of the photol-



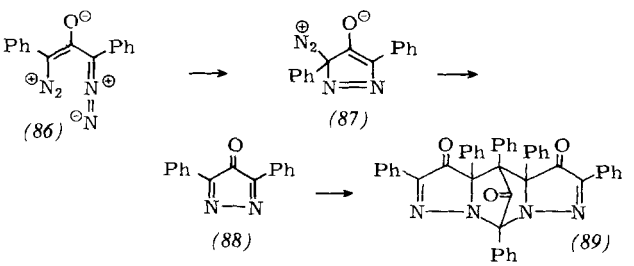
ysis of *(80)* in producing *(82)* is quite interesting in light of *Hoffmann*'s calculations regarding the geometry for singlet carbene additions[45]. These calculations indicate that for a concerted cycloaddition the p orbital of the carbene overlaps in a σ manner with one end of the ethylene π bond. This lopsided configuration is unattainable in the carbene derived from *(80)* without severely distorting the rigid bicyclic framework. The authors suggested that the formation of *(82)* might, in fact, proceed by initial 1,3-dipolar addition of the diazo group to the double bond to produce pyrazoline *(81)*. Extrusion of nitrogen from this transient intermediate could then account for the formation of *(82)*. The photoconversion *(80)* → *(81)* would have to occur from some high vibrational level of the ground state since photochemical 1,3-dipolar cycloadditions are symmetry forbidden.

In 1935 it was briefly reported that 3-diazopropene slowly decomposes at room temperature to give pyrazole[46, 47]. Subsequent investigations showed that this is a general reaction of this class of diazo compounds[48–50]. The small ρ value for the cyclization of 1-aryl-3-diazopropenes, the rate enhancement by aryl conjugation with the carbon-carbon double bond, and the relative insensitivity of the reaction rate to structural changes led *Hart* and *Brewbaker*[50] to conclude that cyclization of 3-diazoalkenes to pyrazoles is an intramolecular, concerted 1,3-dipolar cycloaddition.



(83) *(84)* *(85)*

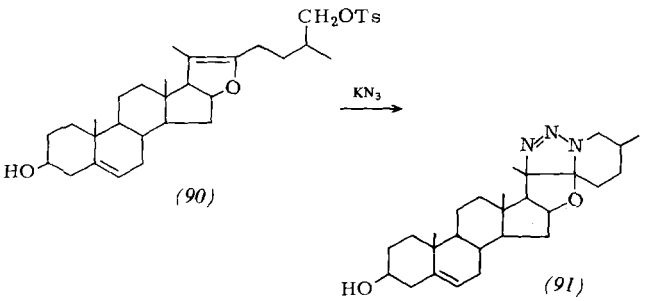
A similar reaction has been reported[51] to occur upon thermal decomposition of the bis-diazo ketone *(86)*. The formation of a trimer *(89)* in this reaction suggested the intermediacy of 3,5-diphenyl-1,2-diaza-4-cyclopentadienone *(88)*. The formation of *(88)* was proposed to involve an electrocyclic ring closure of the bis-diazo ketone *(86)* to give *(87)*, followed by rapid disengagement of nitrogen. The conversion of *(86)* into *(87)* represents another example of the intramolecular cycloaddition of vinyldiazomethanes to pyrazoles[46–50].



(86) *(87)* *(88)* *(89)*

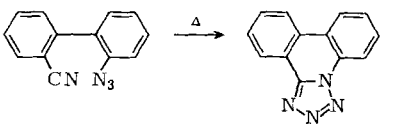
4. Azides

Organic azides are well known to behave as 1,3-dipoles in thermal cycloaddition reactions[1–3]. The first example of this reaction was observed by *Michael* in 1893[52]. With azides, intramolecular cycloadditions have been occasionally reported[53, 54], but systematic data are available only for a series of azidoalkenes[55]. *Uhle* reported that the displacement of the *p*-toluenesulfonate function of the pseudodiosgenin derivative *(90)* with potassium azide in dimethylformamide is followed by 1,3-dipolar cycloaddition to the enol ether olefinic bond to furnish a triazoline derivative *(91)*[53].



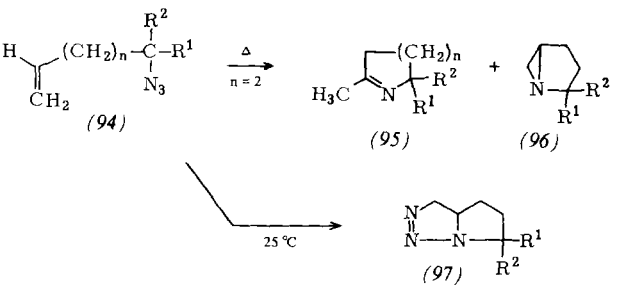
(90) *(91)*

Although less reactive than CC triple bonds, CN triple bonds are known to undergo 1,3-dipolar cycloadditions with some organic azides[5]. The first authenticated case of an azide other than hydrogen azide adding to a nitrile was observed with 2'-azido-2-biphenylcarbonitrile *(92)*[54]. Thermolysis of *(92)* resulted in the formation of tetrazolophenanthridine *(93)*. This transformation can best be described as an intramolecular 1,3-dipolar cycloaddition reaction.



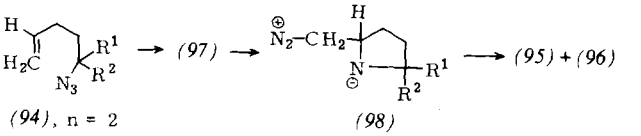
(92) *(93)*

The synthesis and thermal decomposition of various olefinic azides *(94)* to give 1-azabicyclo[3.1.0]hexanes *(96)* and cyclic imines *(95)* has been described by *Logothetis*[55]. The azides were decomposed under a variety of conditions. When the thermolysis was carried out in a hydrocarbon solvent at 80 °C,



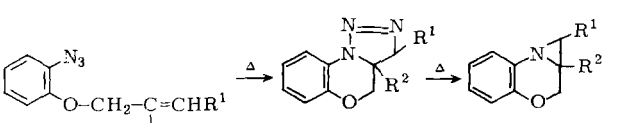
(94) *(95)* *(96)* *(97)*

the decomposition products comprised a mixture of cyclic imines and 1-azabicyclo[3.1.0]hexanes. On the other hand, when the olefinic azides were allowed to stand at 25 °C for 2 months, the isomeric triazolines *(97)* were formed in quantitative yield. Decomposition of the triazolines under conditions identical with the decomposition of the corresponding azides gave *(95)* and *(96)*. On the basis of these results, it was suggested that the triazolines are intermediates in the decomposition of all the olefinic azides studied. Allyl azide and 4-azido-1-pentene cannot undergo internal 1,3-dipolar cycloaddition to give a triazoline similar to *(97)* because of the high degree of strain in such a structure. As a result, their decomposition is very sluggish and no products analogous to *(95)* and *(96)* are formed. The mechanism proposed to explain the formation of *(95)* and *(96)* is outlined below. A nitrene intermediate was completely excluded in these reactions.



(94), n = 2 *(98)*

The intramolecular 1,3-dipolar cycloaddition of aryl azides bearing alkenyl, alkynyl, and nitrile groups has recently been reported by *Fusco et al.*[56]. The decomposition of *(99)* carried out in refluxing benzene gave aziridines *(101)*. The formation of these products involves initial intramolecular cycloaddition

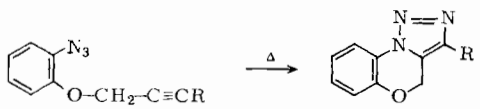


(99) *(100)* *(101)*

$R^1 = R^2 = H$; $R^1 = H$, $R^2 = CH_3$; $R^1 = Ph$, $R^2 = H$

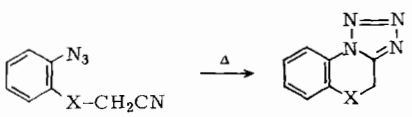
leading to the unstable triazoline system *(100)*. The intervention of such an intermediate was deduced by carrying out the decomposition of *(99)* at room temperature in hexadeuteriobenzene and monitoring the reaction progress by NMR analyses. In addition to the signals of the starting azide and the final product, the spectrum clearly showed a set of signals corresponding to triazoline *(100)*.

Thermolysis of the corresponding alkyne *(102)* gave triazole *(103)* as the only decomposition product. This is the first reported example of the intramolecular cycloaddition of the azido group to an acetylenic function. While the transformation of azide *(102b)* was complete after 3 h, under the same conditions compound *(102a)* entirely disappeared after 15 min. The greater reactivity of *(102a)* in comparison to *(102b)* was somewhat unexpected considering that the conjugated alkynes are usually better dipolarophiles than the unconjugated[57]. The bulky phenyl substituent present in *(102b)* apparently hinders the approach of the reactant groups and consequently decreases the rate of cycloaddition.



(102a), R = H *(103a)*, R = H
(102b), R = Ph *(103b)*, R = Ph

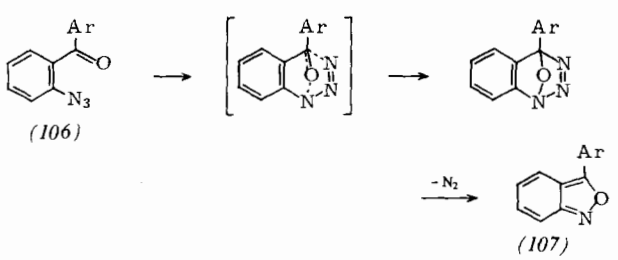
The ring closure of the related azidonitrile system *(104)* has also been studied. The formation of tetrazole derivatives *(105)* was interpreted in terms of an intramolecular 1,3-dipolar cycloaddition. In intermolecular terms, only nitrile groups activated by electron-withdrawing substituents have been shown to behave as dipolarophiles toward azides[5]. The



(104) X = O, CH_2 *(105)*

mutual *ortho* disposition of the two interacting groups in *(104)* provides a favorable stereochemical relationship for intramolecular cycloaddition. Some activating effect by the oxygen atom could be responsible for the greater reactivity in the case X = O.

Ortho-substituted phenyl azides are known to decompose much more rapidly than the corresponding *meta* or *para* isomers. This rate enhancement has been noted primarily in those systems where the *ortho* substituent has some type of α,β-unsaturation and in which the decomposition leads to cyclization. Several workers[58] have suggested that the reaction does not involve a nitrene intermediate but instead proceeds *via* a concerted mechanism in which cyclization and loss of nitrogen are concurrent. On the basis of a kinetic

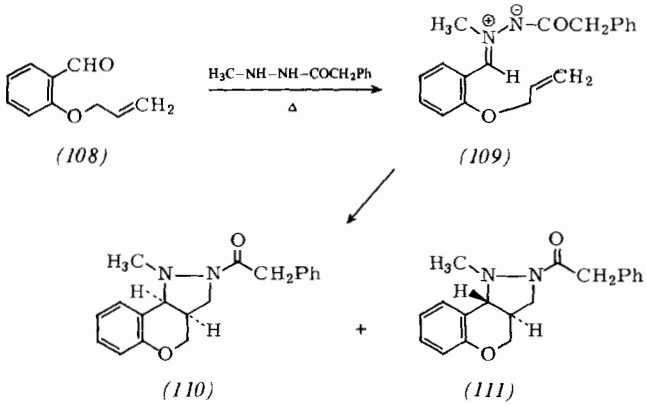


(106) *(107)*

investigation, *Hall et al.*[59] suggested that the cyclization of *o*-azidobenzophenones *(106)* to 3-aryl-2,1-benzoisoxazoles *(107)* can best be explained as proceeding *via* an intramolecular 1,3-dipolar cycloaddition across the carbonyl function. The following mechanism was proposed to account for the kinetic observations.

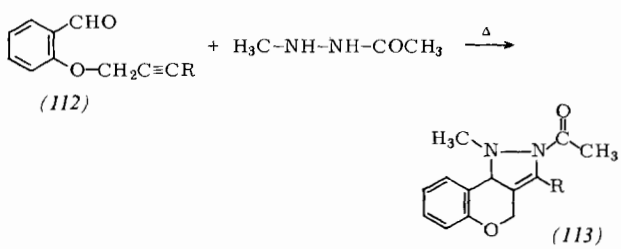
5. Azomethine Imines

These 1,3-dipoles are normally not isolable, but their facile preparation *in situ* from storable precursors makes them easy to use. One convenient procedure for the synthesis of a variety of azomethine imines involves the reaction of 1,2-disubstituted hydrazines with carbonyl compounds[3]. *Huisgen*'s group has shown that the 1,3-dipoles prepared in this fashion are readily intercepted with olefinic dipolarophiles to give pyrazolidines[3]. *Oppolzer*[60] extended this reaction to include systems which contained the olefin and azomethine imine portions in the same molecule[61,62]. For example, treatment of *o*-allyloxybenzaldehyde *(108)* with *N*-methyl-*N'*-phenylacetylhydrazine gave cycloadducts *(110)* and *(111)*. This reaction presumably proceeds through the intermediacy of azomethine imine *(109)* which undergoes a subsequent intramolecular cycloaddition.



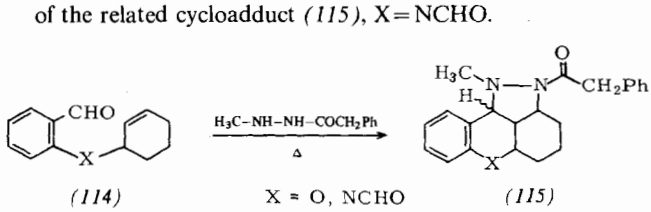
(108) *(109)* *(110)* *(111)*

Similarly, reaction of the related acetylenic derivative *(112)* with *N*-acetyl-*N'*-methylhydrazine gave cycloadduct *(113)* in high yield[62].



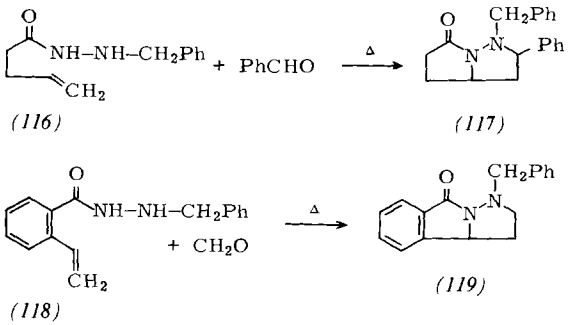
(112) *(113)*

Oppolzer[62] also found that the ether oxygen could be replaced by a formamido group, which results in the formation of the related cycloadduct *(115)*, X = NCHO.



(114) X = O, NCHO *(115)*

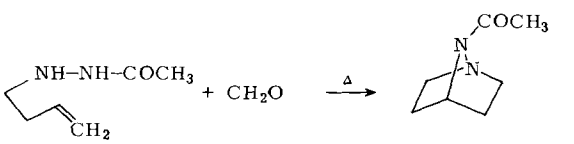
The cyclization was extended to include the reaction of *N*-benzyl-*N'*-(4-pentenoyl)hydrazine *(116)* with benzaldehyde to give cycloadduct *(117)*[61]. Similarly, treatment of *(118)* with formaldehyde produced *(119)*. Both sets of reactions proceed through the intermediacy of an azomethine imine.



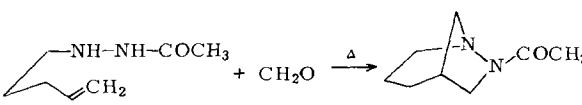
(116) *(117)*

(118) *(119)*

N-Acyl-*N'*-alkylhydrazines react with an aldehyde only on the alkyl substituted nitrogen, thus permitting a regioselective preparation of pyrazolidines with different *N*-substituents. *Oppolzer* showed that the intramolecular 1,3-dipolar cycloaddition reactions of these azomethine imines represent a convenient and simple method for the synthesis of some novel diazabicyclic ring systems. For instance, reaction of *(120)* as well as the homologous olefin *(122)* with formaldehyde gave the 1,7-diazabicyclo[2.2.1]heptane *(121)* and 1,7-diazabicyclo[3.2.1]octane *(123)* in high yield[61].

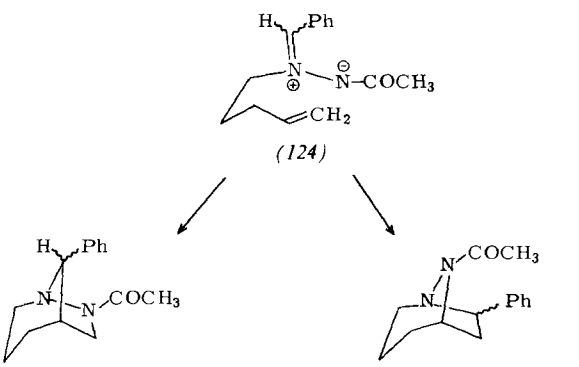


(120) *(121)*



(122) *(123)*

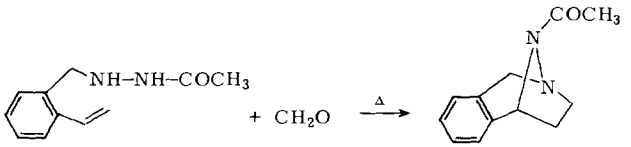
When the condensation was carried out between *(122)* and benzaldehyde, a mixture of two structural cycloadducts was obtained. In this case, cyclization of the transient azomethine imine *(124)* occurs spontaneously and produces a mixture of *(125)* and *(126)*.



(124)

(125), major product *(126)*, minor product

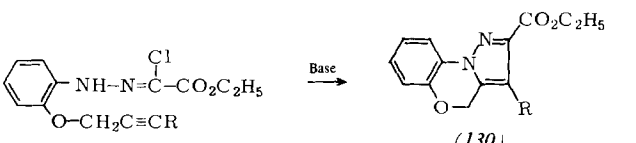
The related *N*-acetyl-*N'*-(*o*-vinylbenzyl)hydrazine *(127)* undergoes a similar intramolecular cycloaddition to produce the partially hydrated 2,5-imino-2-benzazepine *(128)* in 40% yield.



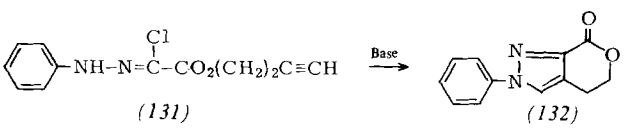
(127) *(128)*

6. Nitrile Imines

Nitrile imines are compounds containing the grouping $R-\overset{\ominus}{N}-\overset{\oplus}{N}\equiv C-R'$. The most convenient method for generation of this class of 1,3-dipoles involves the action of tertiary bases on hydrazidoyl halides such as *(129)* and *(131)*[63]. Here again the 1,3-dipole cannot be isolated and the external dipolarophile must be present in the reaction mixture from the outset. Treatment of *(129)* with base leads to a nitrile imine which can be readily intercepted by the adjacent acetylenic functionality present in the molecule to give the pyrazole *(130)*[64]. Similarly, treatment of *(131)* with base affords cycloadduct *(132)*. These ring closures are particularly interesting in that they involve cycloadditions with unconjugated alkynes, substrates which are generally unreactive toward nitrile imines[65]. Furthermore, while the usual orientation of monosubstituted acetylenes in the intermolecular cycloadducts with nitrile imines is such as to afford 5-substituted pyrazoles[63, 65, 66] obtainment of the 4-substituted pyrazole *(132)* reveals that in a properly chosen substrate the regiospecificity of monosubstituted acetylenes can be inverted.



(129) *(130)*



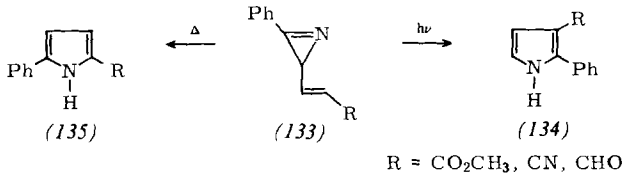
(131) *(132)*

7. Nitrile Ylides

Nitrile ylides are a young but thoroughly investigated class of 1,3-dipoles[1-3]. Access to this class of dipoles can be realized by (a) treatment of imidoyl halides with base[67], (b) thermal or photochemical elimination of phosphoric acid ester from 2,3-dihydro-1,4,2λ^5-oxazaphospholes[68], and (c) photolysis of 2*H*-azirines[69, 70]. The greatest opportunity for structural variation is offered by the latter route. *Padwa*[69] and *Schmid*[70] have independently shown that irradiation of 2*H*-azirines leads to irreversible ring opening and the formation of nitrile ylides as intermediates. These species may be intercepted with a wide variety of dipolarophiles to form five-membered ring heterocycles.

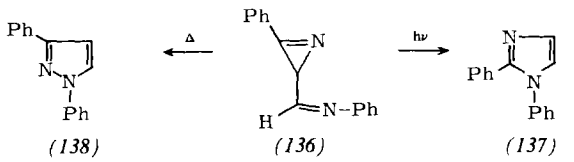
Whereas the cycloaddition of 2*H*-azirines with simple olefins produces 1-pyrrolines, a rearranged isomer can be formed when the alkene and azirine moieties are suitably arranged in the same molecule. This intramolecular cycloaddition was first observed by *Padwa et al.*[71, 72] using 2-vinyl substituted azirines. Irradiation of *(133)* in benzene afforded a 2,3-disub-

stituted pyrrole *(134)* while thermolysis gave a 2,5-disubstituted pyrrole *(135)*. Photolysis of *(136)* proceeded similarly and gave 1,2-diphenylimidazole *(137)* as the exclusive photoproduct. This stands in marked contrast to the thermal reaction of *(136)* which afforded 1,3-diphenylpyrazole *(138)* as the only product.



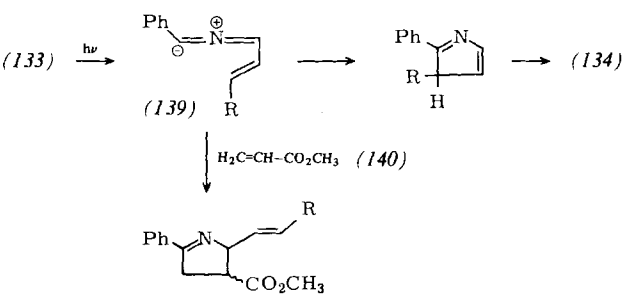
(135) *(133)* *(134)*

R = CO_2CH_3, CN, CHO

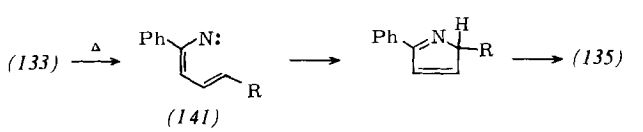


(138) *(136)* *(137)*

The evidence obtained clearly indicates that the photorearrangements of *(133)* and *(136)* proceed by a mechanism which involves a nitrile ylide intermediate. This conclusion was reached by carrying out the irradiation of *(133)* in the presence of a trapping agent *(140)*. Under these conditions, the formation of the 2,3-disubstituted pyrrole *(134)*, which is formed in high yield in the absence of a trapping reagent, is entirely suppressed. Intramolecular cycloaddition of the nitrile ylide intermediate *(139)* followed by a 1,3-sigmatropic hydrogen shift of the initially formed five-membered ring readily accounts for the formation of *(134)* as the final product.

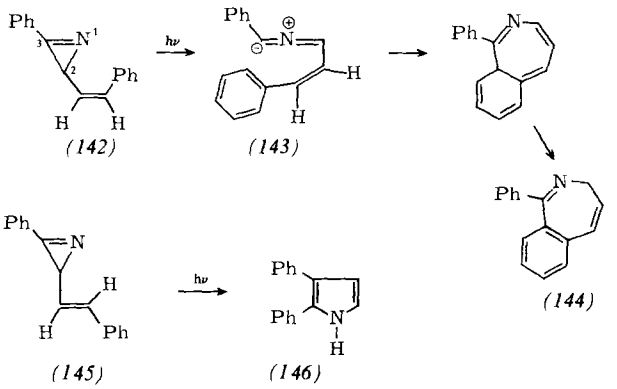


The thermal transformations observed with these systems, on the other hand, have been rationalized in terms of an equilibration of the 2*H*-azirine with a transient vinyl nitrene *(141)* which subsequently rearranges to the 2,5-disubstituted pyrrole.



(141)

In contrast to the photochemical results encountered with *(133)*, the presence of a *cis*-styryl side chain in the 2-position of the azirine ring *(142)* leads to ring expansion and gives benzazepine *(144)*. The 2-[2-(α- and β-naphthyl)vinyl]-3-phenyl-2*H*-azirines behaved similarly and proceeded with complete regiospecificity. The photolysis of the isomeric *trans*-styrylazirine *(145)* took an entirely different course and produced 2,3-diphenylpyrrole *(146)* as the major product. The results indicate that opening of the azirine ring followed by intramolecular cyclization proceeds at a faster rate than *cis*-

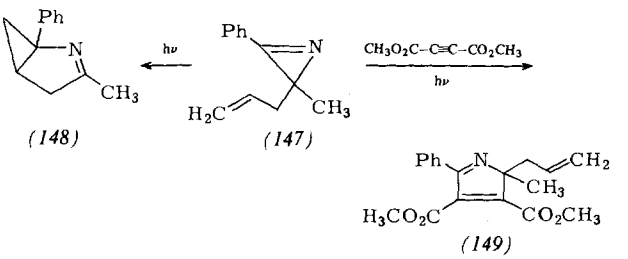


(142) *(143)* *(144)*

(145) *(146)*

trans-isomerization about the CC double bond. The preference for cyclization of *(143)* to a seven-membered ring was attributed to stereoelectronic factors. Closure of the linear dipolar intermediate *(143)* obtained from *(142)* occurs more easily *via* a seven-membered transition state and leads to the preferential formation of benzazepine *(144)*. Cyclization of the nitrile ylide derived from the *trans* isomer to a seven-membered ring is precluded on structural grounds and formation of 2,3-diphenylpyrrole *(146)* occurred instead.

Nitrile ylides have been classified by *Huisgen*[1-3] as nitrilium betaines, a class of 1,3-dipoles containing a central nitrogen atom and a CN π-bond orthogonal to the 4π-allyl system. Among the possible resonance forms of a nitrile ylide, a carbene structure can be envisioned which makes conceivable a 1,1-cycloaddition of this 1,3-dipole. Recently, *Padwa* and *Carlsen* reported the first example of such a cycloaddition[73].

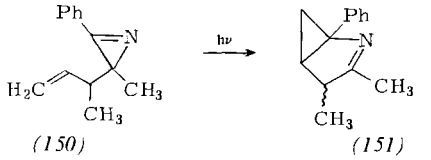


(148) *(147)* *(149)*

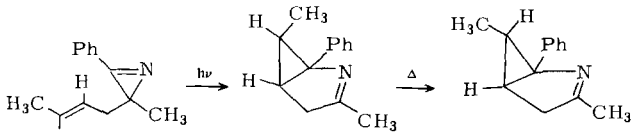
These authors found that irradiation of 2-allyl-2-methyl-3-phenyl-2*H*-azirine *(147)* gave 3-methyl-1-phenyl-2-azabicyclo[3.1.0]hex-2-ene *(148)* as the exclusive photoproduct. Photolysis of *(147)* in the presence of excess dimethyl acetylenedicarboxylate resulted in the trapping of the normal nitrile ylide and afforded cycloadduct *(149)* in high yield. Under these conditions, the formation of *(148)*, which is produced in quantitative yield in the absence of a trapping reagent, was entirely suppressed.

The photoreactions of the closely related methyl-substituted azirines *(150)* and *(152)* were also examined. Irradiation of *(150)* produced azabicyclohexene *(151)* while photolysis of *(152)* gave the analogous compound *(153)* as the primary photoproduct. Upon standing at room temperature, *(153)* epimerized to the thermodynamically more stable *exo*-isomer *(154)*.

The formation of the photoproducts *(148)*, *(151)*, and *(153)* was found to be completely suppressed when the irradiations were carried out in the presence of methyl acrylate *(140)*. The only products formed under these conditions were the usual 1-pyrrolines.

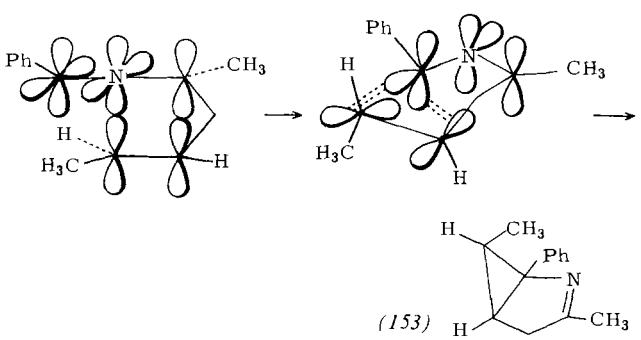


(150) (151)



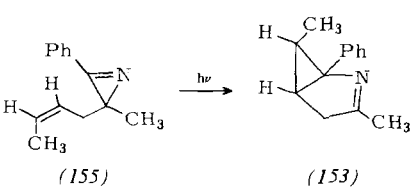
(152) (153) (154)

Padwa and *Carlsen*[73] have pointed out that bimolecular 1,3-dipolar additions proceed *via* a "two-plane" orientation complex in which the dipole and dipolarophile approach each other in parallel planes[1-3]. In order to achieve this type of transition state, the linear nitrile ylides derived from the irradiation of these allylazirines must first bend. This involves disruption of the orthogonal π bond at some modest energy cost but leaves the allyl anion π system undisturbed. The cycloaddition of allylazirines *(147)*, *(150)*, and *(152)* with added dipolarophiles proceeds in this fashion and affords 1-pyrroline derivatives [*e.g. (149)*] as the primary cycloadducts. Inspection of molecular models of the allyl substituted nitrile ylides indicates that the normal "two-plane" orientation approach of the linear nitrile ylide and the allyl π system is impossible as a result of the geometric restrictions imposed on the system. Product formation is possible, however, if the linear nitrile ylide undergoes rehybridization to give a species of bent geometry which subsequently undergoes 1,1-cycloaddition with the neighboring double bond. The most favorable transition state for the 1,1-cycloaddition reaction is one in which the π-orbitals of the nitrile ylide and olefinic double bond are orthogonal. This orthogonality could, in principle, permit the occurrence of a concerted orbital symmetry-allowed [$_{\omega}2_s+_{\pi}2_a$] process and thus accommodate the formation of the thermodynamically less favored *endo* isomer *(153)*.

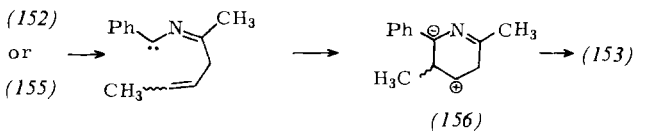


(153)

More recent work[74], however, has shown that irradiation of the *cis*-substituted azirine *(155)* also produced azabicyclohexene *(153)*. This observation indicates that the 1,1-cycloaddition process is stereoselective but not stereospecific. A reasonable explanation to account for the observed stereoselectivity is that the 1,1-cycloaddition process occurs by initial attack of the carbene carbon on the terminal position of the double bond. Such an attack will generate a six-membered ring dipole *(156)* which contains a secondary carbenium ion



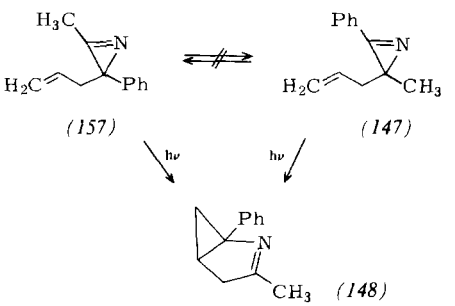
(155) (153)



(152) or (155) (156) (153)

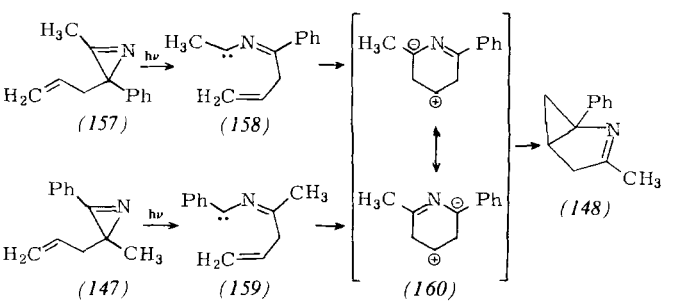
as well as an azaallyl anion portion. Collapse of this new 1,3-dipole to the thermodynamically favored *exo* product *(154)* will result in a severe torsional barrier on closure. On the other hand, collapse to the thermodynamically less favored *endo* isomer *(153)* moves the phenyl and methyl groups increasingly further apart and would account for the formation of the less stable product.

Supporting evidence for this suggestion was obtained by irradiating the isomeric 3-methyl-2*H*-azirine system *(157)*. Photolysis of this azirine results in the quantitative formation of azabicyclohexene *(148)*. This is the same azabicyclohexene that was formed from the irradiation of azirine *(147)*. A control experiment showed that *(147)* and *(157)* were not interconverted under the photolytic conditions.



(157) (147) (148)

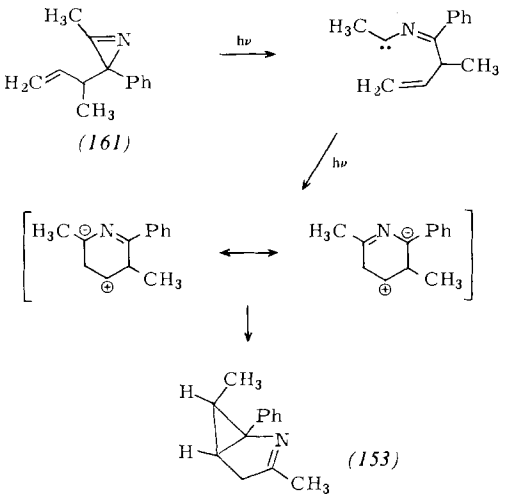
The formation of *(148)* from *(157)* is perfectly consistent with the generation of a six-membered ring dipole *(160)*. Thus, cyclization of the initially formed carbene *(158)* generates *(160)* which closes to azabicyclohexene *(148)*. The same six-membered ring dipole is also formed from azirine *(147)*.



(157) (158) (148) (147) (159) (160)

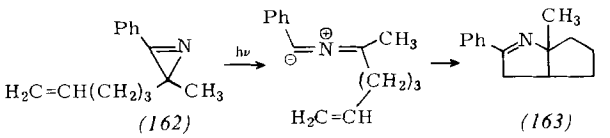
Thus the stereoselectivity observed with azirines *(152)* and *(155)* as well as the regiospecificity encountered with azirines *(147)* and *(157)* can be attributed to a two-step cyclization path which involves a six-membered ring dipole. The formation of *endo*-azabicyclohexene *(153)* from methylazirine *(161)* provides additional support for this interpretation.

When the chain between the azirine ring and the alkene end is extended to three carbon atoms, the normal mode of 1,3-intramolecular dipolar cycloaddition occurs. For example, irradiation of azirine *(162)* gave 1-pyrroline *(163)*



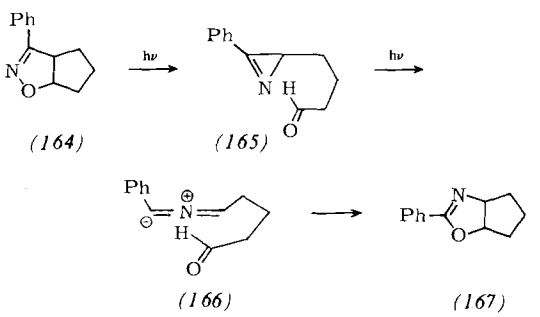
(161) (153)

in quantitative yield[75]. In this case, the methylene chain is sufficiently long to allow the dipole and olefinic portions to approach each other in parallel planes.



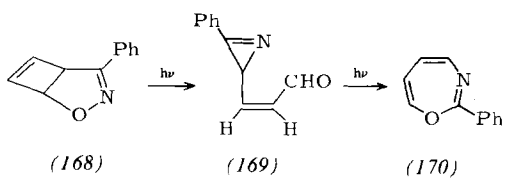
(162) (163)

In a related case, *Schmid et al.* reported on the photoisomerization of 2-isoxazoline *(164)* to oxazoline *(167)*[76]. The reaction was proposed to proceed *via* a transient azirine *(165)*. This intermediate was not isolated but was suggested to undergo rapid ring opening to nitrile ylide *(166)* which cyclized to the observed photoproduct *via* an internal 1,3-dipolar cycloaddition reaction.



(164) (165) (166) (167)

The related 4-phenyl-2-oxa-3-azabicyclo[3.2.0]hepta-3,6-diene *(168)* system undergoes a similar photochemical rearrangement to produce 2-phenyl-1,3-oxazepine *(170)*[77]. This reaction has been proposed to involve an azirine intermediate *(169)* which subsequently cyclizes to the observed product.

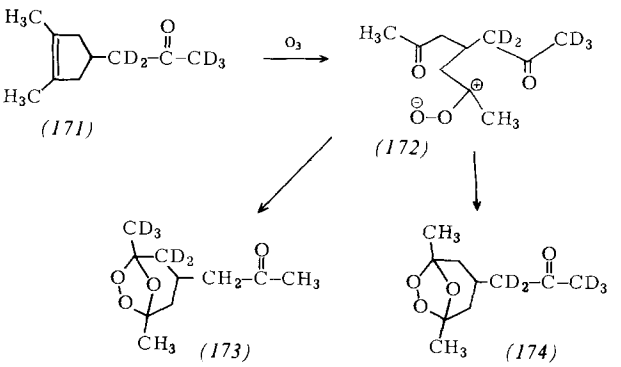


(168) (169) (170)

When the chain between the azirine ring and olefinic portion is reduced to two carbon atoms, no cycloadduct was obtained. In this case, the "two-plane" orientation approach of the linear nitrile ylide and the π system is too difficult to attain and other competing processes occur[75].

8. Carbonyl Oxides

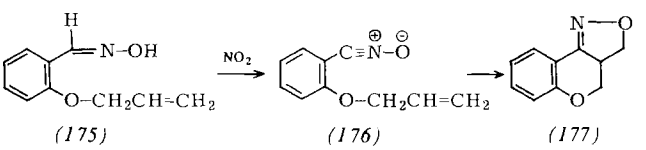
Carbonyl oxides (Criegee zwitterions) have never been isolated, but indirect evidence for their existence is abundant[78, 79]. These unusual species are usually generated by ozonolysis of a suitable olefin, although more recent evidence has been presented for their formation by reaction of a carbene with oxygen[80]. *Criegee* presented evidence which indicates that ozonides may be formed by the 1,3-dipolar addition of carbonyl oxides to carbonyl compounds[78]. Some recent work by *Criegee*'s group has shown that the ozonolysis of 1,2-disubstituted 1-cyclopentenes, *e. g. (171)*, containing different substituents in the 4-position of the ring produces carbonyl oxides such as *(172)* as reaction intermediates[81]. These dipoles undergo intramolecular 1,3-dipolar cycloaddition with each of the two functional groups present. Thus two different ozonides are formed, in the present case *(173)* and *(174)*.



(171) (172) (173) (174)

9. Nitrile Oxides

1,3-Dipoles of this class can be conveniently generated by the base treatment of hydroxamic acid chlorides or by oxidation of aldoximes[82]. Numerous cycloadditions involving nitrile oxides had already been described when the general concept of 1,3-dipolar cycloadditions was formulated by *Huisgen et al.*[1]. Oxidation of 2-allyloxybenzaldehyde oxime *(175)* by nitrogen dioxide has recently been reported to give the fused ring compound *(177)*, the product of an intramolecular cycloaddition of the intermediate nitrile oxide *(176)*[83].

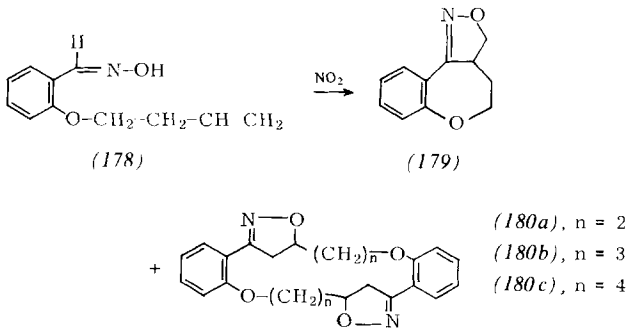


(175) (176) (177)

Nitrile oxides generally undergo bimolecular 1,3-dipolar cycloaddition with terminal double bonds to give 5-substituted 2-isoxazolines[82, 84, 85]. Obtainment of the 4-substituted 2-isoxazoline *(177)* in the intramolecular cycloaddition of *(175)*, indicates that geometrical factors can force the reaction to occur in the opposite manner from that normally encountered.

This observation led *Garanti et al.* to examine the intramolecular 1,3-dipolar cycloaddition reaction as a function of chain length between the dipole and dipolarophile[86]. Treatment of aldoxime *(178)* with nitrogen dioxide gave a mixture of *(179)* (17%) and *(180a)* (2%).

With the next higher homologs, the reaction afforded compounds *(180b)* and *(180c)* together with a sizable quantity of uncharacterized resinous material. These results clearly



(178) (179)

(180a), n = 2
(180b), n = 3
(180c), n = 4

indicate that the chain length between the dipole and dipolarophile groups has a substantial effect on the intramolecular cycloaddition. Thus, while aldoxime *(175)* gave *(177)* in 42% yield, formation of *(179)* from *(178)* occurred to a minor extent (17%) and no internal adduct could be obtained from the next higher homologs. The formation of the large ring compounds *(180a)*—*(180c)* involves an initial intermolecular cycloaddition to give long chain intermediates which are capable of undergoing a subsequent intramolecular ring closure to the final product.

10. Conclusion

Intramolecular 1,3-dipolar cycloaddition is an extremely versatile and important reaction. The range of synthetic possibilities which it opens for the construction of fused heterocycles is extremely large. A number of dipoles which undergo this reaction have been summarized and the general outlines and potential analogies for these reactions noted. Further work will be needed to clarify some of the mechanistic features. The development of general synthetic routes leading to new heterocyclic systems using this reaction offers considerable challenge and promise.

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The Fischer-Tropsch Synthesis: Molecular Weight Distribution of Primary Products and Reaction Mechanism

By G. Henrici-Olivé and S. Olivé[*]

An evaluation of literature data concerning the production of hydrocarbons and alcohols by the Fischer-Tropsch procedure indicates that the molecular weight distribution of the primary products can be described by the Schulz-Flory equation ("normal" or "most probable" distribution). It follows that the highest attainable selectivity for a given molecular weight range can be calculated. A reaction mechanism is suggested.

1. Introduction

The oil embargo, and the escalation in price of crude oil, have brought about a considerable increase in the price of oil-based raw materials such as paraffins, olefins, alcohols, *etc.* Although the eventual exhaustion of petroleum resources has been predicted for a considerable time, the present shortage actually occurred several years earlier than expected, and the chemical industry, with its current reliance on oil-based raw materials, is particularly affected.

As oil becomes more and more expensive, chemists revert to coal as a source of carbon which had almost been forgotten in the course of the years. Some fifty years ago, however, German chemists were already confronted with the same problem. Germany, possessing huge stocks of coal, but completely inadequate oil resources, was forced to undertake the transformation of coal into liquid hydrocarbons. As early as 1924, *Franz Fischer* published a book on this subject[1]. In the succeeding decades two processes were simultaneously developed to great industrial importance: the catalytic hydrogenation of coal at high pressure (Bergius process), and the catalytic synthesis of hydrocarbons from carbon monoxide and hydrogen, obtained from coal and water, at normal and medium pressure (Fischer-Tropsch process). During World War II this development reached its zenith.

After 1945 the situation changed. European pre-embargo prices of oil and coal were comparable (about \$ 30—40 per ton), but coal has an unfavorable TOE (ton of oil equivalent): 1 ½ tons of coal supply the same energy as 1 ton of oil. Moreover, the ease of automating transport systems and feedlines for refineries, production plants, industrial and domestic heating, *etc.* has helped oil to oust the dirty and inconvenient material coal. Even at present-day prices of about \$ 100 per ton of petroleum *versus* \$ 70—80 per ton of coal, the production of gasoline from coal does not appear immediately attractive. However, one of the sound effects of the embargo shock has been to create a feeling of responsibility for the future. Apart from the search for other sources of energy such as nuclear, geothermal, water, and wind power, scientific and industrial investigations turn back to coal.

The present study describes some possibilities and limitations of the synthesis of hydrocarbons and alcohols from CO and H_2 (Fischer-Tropsch synthesis). Moreover, an estimate is made of how much product of a given degree of polymerization may be expected in the most favorable case. The basis of this estimate is the observation that products obtained by this process exhibit a characteristic distribution of chain length, as we found during the evaluation of literature data. We have applied concepts originating in the field of molecular catalysis with defined transition metal complexes and from polymer chemistry to mechanistic details reported by various authors, and suggest a reaction mechanism for the Fischer-Tropsch synthesis.

2. Development and Present Status of the Fischer-Tropsch Synthesis

At the beginning of the synthesis of hydrocarbons from CO and H_2 stands the classical methane synthesis of *Sabatier* and *Senderens* in 1902[2], but it was not until 1922 that *Fischer* and *Tropsch* obtained their first patent on "Synthol", a mixture of oxygen-containing derivatives of hydrocarbons, produced from CO and H_2 at over 100 atm and at 400 °C, with alkali-treated iron shavings as catalyst[3]. There are several competent review articles describing the further development of the Fischer-Tropsch synthesis[4], which we do not intend to duplicate. We shall restrict ourselves to some highlights, with emphasis on the present status.

In 1925 *Fischer* and *Tropsch* succeeded in directing the synthesis to give predominantly hydrocarbons; they patented a normal pressure process, operating in the temperature range 250—300 °C, and using Fe/ZnO or Co/Cr_2O_3 as catalyst[5]. In 1936/37 *Fischer* and *Pichler* found that working at medium pressure (5—30 atm), with cobalt[6] or iron[7] catalysts, substantially improved yield and catalyst lifetime. Using a ruthenium catalyst, and working at high pressure (1000—2000 atm) and temperature (140—200 °C), *Pichler et al.* could orient the synthesis to high melting linear paraffins having molecular weights up to 10^6[4d, 8]; the "polymethylenes" obtained are practically identical with Ziegler polyethylene.

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More recently, interest appears to have shifted back towards the original oxygen-containing products of the first "Synthol" process. High pressure and high temperature processes have been reported to give aliphatic alcohols in the C_1—C_{18} range, important raw materials for detergents, plasticizers, *etc.*[9]. In recent Russian Patents[9d], iron catalysts have been used, at temperatures in the range 160—220°C, pressures of 50—300 atm, and $H_2/CO = 5:1$ to 20:1, to produce liquid oxygen-containing compounds in the range C_1—C_{20}, mostly alcohols. Subsequent hydrogenation over Cu/Cr catalysts increases the yield of alcohols. At high space velocity, selectivities up to 86% (expressed as percentage of alcohols in total liquid product boiling below 160°C) are claimed[9e].

This brief summary may, at the same time, give an impression of the versatility of the Fischer-Tropsch synthesis: depending upon catalyst, pressure and temperature, the process can be oriented predominantly to liquid hydrocarbons, waxes, or alcohols. Nevertheless the oil-based processes for the production of these chemicals have replaced the Fischer-Tropsch synthesis almost completely for the reasons mentioned in Section 1. The only important industrial plant for the production of gasoline, gas oil, and paraffins from coal by the Fischer-Tropsch procedure is located in South Africa, where the price of coal is still very attractive (about 1/6 of that in Western Germany, in 1970[4d]). The South African Coal, Oil and Gas Corporation Ltd. (Sasol) uses an intermediate pressure process (20—25 atm), with iron catalysts. Fixed bed and circulating catalyst procedures have been developed there to high technical maturity. Table 1 and 2 compare the products obtained by the two processes[4d].

Table 1. Comparison of the products obtained with fixed bed catalyst and with circulating catalyst (in weight-%) [4d].

Fraction	Fixed bed catalyst (220—240°C)	Circulating catalyst (310—340°C)
C_3—C_4	5.6	7.7
C_5—C_{11} (gasoline)	33.4	72.3
Gas oil	16.6	3.4
Paraffin, m.p. <60°C	22.1	3.0
Paraffin, m.p. 95—97°C	18.0	—
Alcohols, ketones	4.3	12.6
Acids	traces	1.0

The iron catalyst for the fixed bed process is prepared by precipitation of iron hydroxide with silica gel. The process operates at 220—240°C, 25 atm, and at a H_2/CO ratio of 1.8:1. A conversion of about 70% per pass (referred to carbon) is obtained. The catalyst for the circulating catalyst procedure is produced by melting iron oxide and additives in an electric furnace at 1500°C and milling the melt to a fine powder; the latter is circulated in the reaction volume, impelled by the incoming gas stream. (Reaction conditions: 310—340°C; 24 atm; $H_2/CO = 6:1$). The conversion per pass (referred to CO) is >90%. This process gives a considerably lower average molecular weight of the products, with a maximum in the gasoline range, and a higher content of oxygen containing derivatives (Table 1). Furthermore, there is a remarkably high fraction of olefins in the product (Table 2). The fixed bed process, on the other hand, gives a higher content of gas oil and waxy paraffins, alkenes and alkanes being present in comparable amounts. In fact, Sasol operates a combination of both processes, which permits a flexible adaptation to market requirements.

Table 2. Comparison of the composition of the liquid fraction for fixed bed catalyst and circulating catalyst (in vol.-%) [4d].

Components	Fixed bed catalyst		Circulating catalyst	
	C_5—C_{10}	C_{11}—C_{18}	C_5—C_{10}	C_{11}—C_{18}
Olefins	50	40	70	60
Paraffins	45	55	13	15
Oxygen-containing compounds	5	5	12	10
Aromatics	-	—	5	15

3. The Primary Products

The synthesis of hydrocarbons involves stepwise incorporation of one carbon atom at a time with simultaneous formation of water, according to the overall equation:

$$n\mathrm{CO} + 2n\mathrm{H_2} \rightarrow (\mathrm{CH_2})_n + n\mathrm{H_2O} \quad (1)$$

The mixture generally contains paraffins, olefins, alcohols, aldehydes, acids, esters and aromatic compounds in varying amounts. Even in the early days of the process[10, 11] it was found that the main products obtained with cobalt catalysts were linear olefins and paraffins, and that the small amount of nonlinear products consisted predominantly of monomethyl branched compounds. Since olefins and paraffins were found to have the same carbon skeleton, it was assumed that the olefins are the primary products of the synthesis, and that the paraffins are formed therefrom by subsequent hydrogenation.

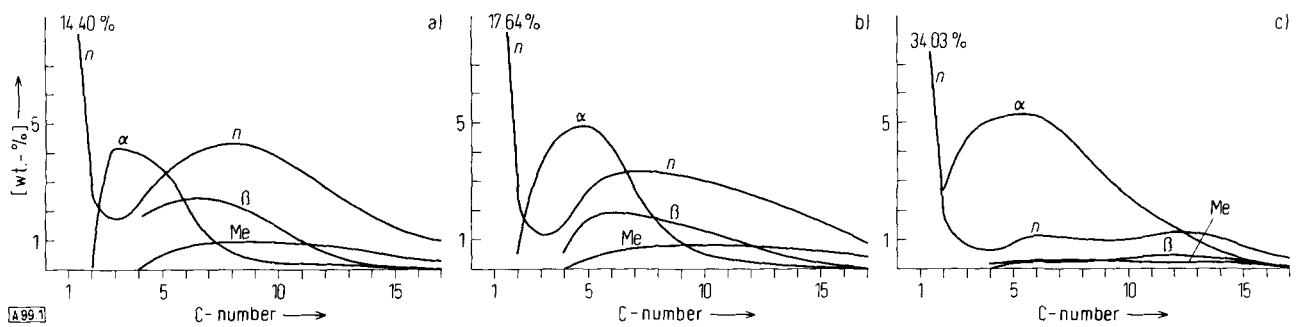


Fig. 1. Composition of the Fischer-Tropsch mixture of hydrocarbons as a function of the space velocity: a) 78 h^{-1}, b) 337 h^{-1}, c) 2380 h^{-1}. n = n-paraffins, α = α-olefins, β = β-olefins, Me = methyl-paraffins. Catalyst = Co/ThO_2 (after [14]). The space velocity is defined as the volume of synthesis gas pervolume of catalyst and hour.

The olefinic component of the hydrocarbons consists mainly of α- and β-olefins (1- and 2-alkenes). The fact that the concentration of α-olefins is generally much higher than that corresponding to the thermodynamic equilibrium led *Friedel* and *Anderson*[12] to the conclusion that α-olefins should be the primary products of the synthesis.

This conclusion was confirmed by *Pichler et al.*[13], who were able to show that the α-olefins content of the product increases with increasing space velocity of the synthesis gas feed. This observation is represented in Figure 1. At longer residence time (low space velocity) the primarily formed α-olefins are transformed in secondary reactions into β-olefins, linear paraffins, and methyl-branched products. In all cases there is a remarkably high content of methane.

In contrast to the secondary products mentioned, the alcohol fraction among the products was found to be independent of space velocity. *Pichler et al.*[14] concluded convincingly that the alcohols are also primary products of the process. The authors indicated that there might be a common precursor for linear α-olefins and linear alcohols.

4. Secondary Reactions of the α-Olefins

The development of more efficient gas chromatographic methods (capillary columns, radio gas chromatography) has recently permitted a detailed determination of the many isomers contained in the synthesis products, and hence provided an insight into the course of the secondary reactions. *Pichler et al.*[15,4d] reported a complete analysis of the C_7 hydrocarbon fraction of Sasol's fixed bed catalysis product. The authors showed that this fraction is >91 % linear, and that the nonlinear part is >90 % monomethyl-, 6 % dimethyl- and 2.5 % ethyl-branched. The approximative composition of the linear part is 51 % heptane, 31 % 1-heptene, 17 % *cis*- and *trans*-2-heptene, and only 1 % *cis*- and *trans*-3-heptene.

Another important contribution towards the mechanism of the secondary reaction of the α-olefin was made by *Schulz et al.*[16]: ^{14}C-tagged ethylene, propylene, 1-butene, or 1-hexadecene were added to the synthesis gas, and the fate of these α-olefins was monitored by radio gas chromatography. With cobalt catalysts over 90 % of the added olefin reacts. With iron systems the reaction is somewhat slower. Most of the olefin is converted to alkane by hydrogenation. But α-olefins are also incorporated into the growing chain, or they can start a new chain. With increasing molecular weight the incorporation of the α-olefins decreases, as expected from their polymerization chemistry; it is significant only for ethylene and propylene. The incorporation of ethylene does not lead to branching, that of propylene gives methyl branches.

Simultaneously, α-olefins are split, with breaking of the double bond. Since this splitting occurs in a hydrogen atmosphere, additional methane is formed by this secondary process. With some 0.5 vol.% of [1-^{14}C]-1-alkene in the feed, 4—9% of the ^{14}C was found as methane in the product. Interestingly also [2-^{14}C]-propene gave a considerable amount of tagged methane. Hence the above decomposition reactions [(a)—(c)] have to be considered.

$$H_2C{=}CH_2 \longrightarrow 2\ CH_4 \qquad (a)$$

$$H_3C{-}CH{=}CH_2 \longrightarrow \begin{cases} H_3C{-}CH_3 + CH_4 \\ 3\ CH_4 \end{cases} \qquad (b)$$

$$R{-}CH{=}CH_2 \longrightarrow R{-}CH_3 + CH_4 \qquad (c)$$

The splitting of the olefins is more important with cobalt catalysts than with iron systems (cf. the high methane content in Fig. 1). The opposite is true for the incorporation reaction.

Neither Co nor Fe produce significant cracking of the paraffins. ^{14}C-tagged butane added to the synthesis gases could be recovered unchanged in over 99 % yield.

5. Distribution of the Molecular Weights

Figure 2 shows a typical distribution curve of the hydrocarbons obtained with a cobalt catalyst[14]. With the exception of the high methane content, the curve is strongly reminiscent of the Schulz-Flory distribution of molecular weights, frequently found in oligomerization and polymerization processes ("most-probable" or "normal" distribution). As an example, the oligomerization of ethylene, where chain propagation and chain transfer are the main reactions determining the distribution of molecular weights, was treated recently[17].

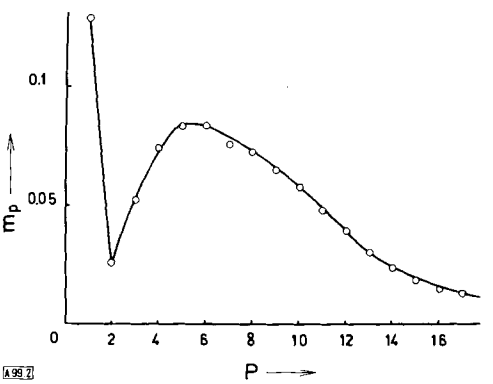


Fig. 2. Distribution of chain lengths of hydrocarbons; run a) of Fig. 1 (cf. Ref. [14]). m_P = weight fraction of oligomers having degree of polymerization P (= number of C atoms).

Fischer-Tropsch synthesis is actually a polymerization (oligomerization) process, where the "monomer" is replaced by $(CO+2H_2)$ [see Eq. (1) in Section 3]. Consequently, we may treat this process in terms of polymerization kinetics, as outlined formerly for ethylene oligomerization.

Although the chain propagation is a multistep reaction (see Section 6), its rate (r_p) may be defined from a kinetic point of view, as

$$r_p = + \frac{d[-CH_2-]}{dt} \qquad (2)$$

In typical Fischer-Tropsch synthesis, the rate of propagation r_p remains constant over weeks, *i.e.* we may assume that the concentration of active centers remains constant. This means that no termination reactions leading to annihilation of the growing centers take place. If one further takes into account that the number of chains produced is by far greater than the number of active centers, it appears evident that the reaction interrupting the chain growth and leading to oligomers has to be a chain transfer reaction, in the course of which the chain leaves the metal, and a new chain can be started at the metal. Since the primary compounds are

α-olefins, the carrier of the kinetic chain has to be a metal hydride. The chain transfer reaction can be described as

$$R{-}CH_2{-}CH_2{-}Metal \rightleftarrows R{-}CH{=}CH_2 + H{-}Metal$$

and is assumed to be of the same nature as the well known β-hydrogen abstraction, observed frequently with soluble transition metal-alkyl complexes (see, *e.g.*[17]). Its rate (r_{tr}) is given by Eq. (3). The metal hydride continues the kinetic chain (cf. Section 6).

$$r_{tr} = + \frac{d[\text{Olefin}]}{dt} \tag{3}$$

The Schulz-Flory distribution of molecular weights is given by[18][*]:

$$m_P = (\ln^2 \alpha) P \alpha^P \tag{4}$$

where m_P represents the weight fraction of the oligomers of a certain degree of polymerization P (here number of carbons in the chain). α is the probability of chain growth defined as

$$\alpha = \frac{r_p}{r_p + r_{tr}} \tag{5}$$

Eq. (4) can be expressed in logarithmic form

$$\log \frac{m_P}{P} = \log(\ln^2 \alpha) + P \log \alpha \tag{6}$$

If for a given polymer the graphical representation of $\log(m_P/P)$ *versus* P gives a straight line, and α, as determined from the slope ($=\log\alpha$) and from the intercept with the ordinate [$=\log(\ln^2\alpha)$], are in good agreement, the molecular weight distribution of this polymer obeys the Schulz-Flory distribution law.

Unfortunately only few distributions suitable for evaluation have been reported in the literature. They are, however, sufficient to give a definite answer.

Figures 3 and 4 refer to Fischer-Tropsch syntheses oriented towards the production of hydrocarbons. Since the primary α-olefins are partly transformed into inner olefins (isomerization) and paraffins (hydrogenation), the weight fraction m_P for each degree of polymerization is the sum of olefins and paraffins of the same number of carbons. Figure 3 is a plot of the data of Figure 2 according to Eq. (6). In the range C_4—C_{12}, the experimental points lie on a straight line. C_1 is too high and C_2 and C_3 are too low, as are the values beyond C_{13}. The value of α is 0.81 from the slope, and 0.80 from the intercept.

Figure 4 shows the same plot for data of *Anderson et al.*[4b]. The range C_3—C_{13} gives a reasonable straight line. Again here the value of C_1 is too high and the values of C_2 and beyond C_{13} are too low. From the slope a value of $\alpha = 0.87$ is obtained; from the intercept $\alpha = 0.86$.

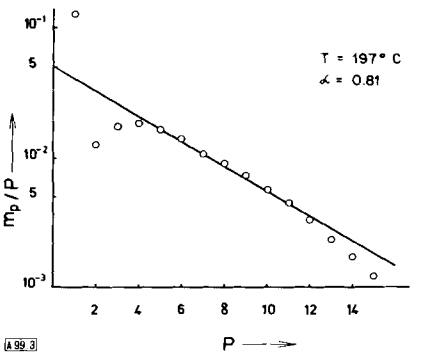


Fig. 3. Plot of hydrocarbon data of Fig. 2 according to Eq. (6).

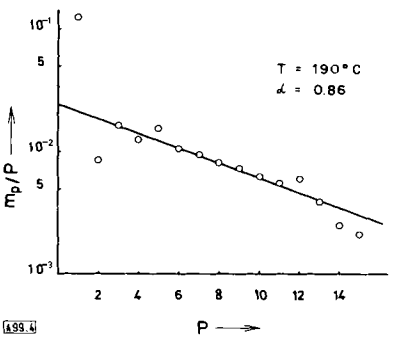


Fig. 4. Hydrocarbon data (after [4b]) represented according to Eq. (6). Cobalt catalyst.

The reasons for the deviations in the range C_1—C_3 have already been mentioned: the α-olefins with the greatest ability to be coordinatively bonded to a transition metal (ethylene > propylene) are partly lost by decomposition to methane and, to a lesser extent, by incorporation into growing chains. At the upper end of the distribution, the hydrocarbons formed tend to have longer residence times on the catalyst due to their lower mobility. Presumably they are partly polymerized, partly cracked, or even carbonized. An additional uncertainty in this range may be caused by the fact that the high boiling fractions give very broad peaks on gas chromatography; their values tend to be underestimated[17].

As mentioned in Section 2, the Fischer-Tropsch synthesis can be oriented to give predominantly alcohols, by proper selection of catalyst and reaction conditions. Using the data of *Kagan et al.*[9e], we applied Eq. (6) also to alcohols. Figure 5 shows two sets of data, obtained with different catalysts. For the Fe_3O_4 catalyst modified with Al_2O_3 and K_2O (Fig. 5a) an average value of $\alpha = 0.37$ has been calculated, from the slope (0.38) and from the intercept (0.36). Data of the pure Fe_3O_4 system (Fig. 5b) give the same value, $\alpha = 0.54$, from slope and intercept.

The examples show that the molecular weight distribution of the products of Fischer-Tropsch syntheses are of the Schulz-Flory type. This fact permits calculation of the maximum selectivity for a certain molecular weight range for a given α, making use of Eq. (4)[17]. In Figure 6, curve a represents the sum of products C_4—C_{10} ($\sum C_4$—C_{10}) as a function of α. The range C_4—C_{10} was chosen as an interesting one for olefins and alcohols. Of course, any other range can easily be computed. The curve indicates that the highest possible amount of C_4—C_{10} to be obtained will represent about 50% of the total amount of olefins (or alcohols) produced, at a

[*] Eq. (4) is the version given by *G. V. Schulz*; the distribution function given by *Flory* reads, with the present nomenclature:

$$m_P = (1-\alpha)^2 P \alpha^{P-1}$$

At $\alpha \geq 0.5$ both equations are equivalent [18]. For the presently intended determination of α from a graphical evaluation of experimental fractionation data, both equations give identical results.

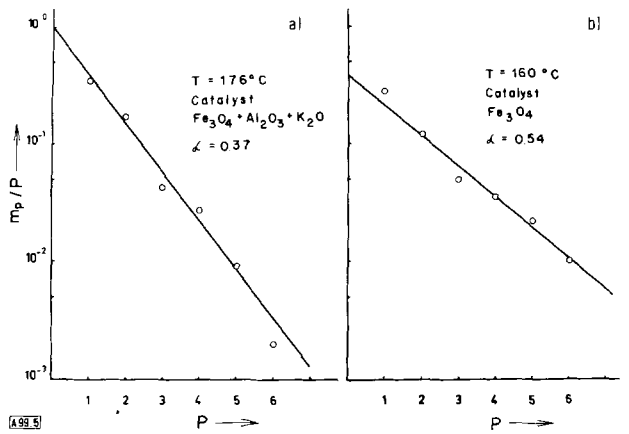


Fig. 5. Molecular weight distributions of alcohols (after [9e]) represented according to Eq. (6).

value of $\alpha \approx 0.7$. It may be noted that under these conditions C_1—C_3 is about 35%, and $>C_{10}$ about 15% of the total product. Curve b shows the sum of the products C_2—C_4 ($\sum C_2$—C_4) also as a function of α. The maximum attainable corresponds to about 56% at a value of $\alpha \approx 0.45$. A large amount of C_1 and small amounts of products higher than C_4 constitute the remainder.

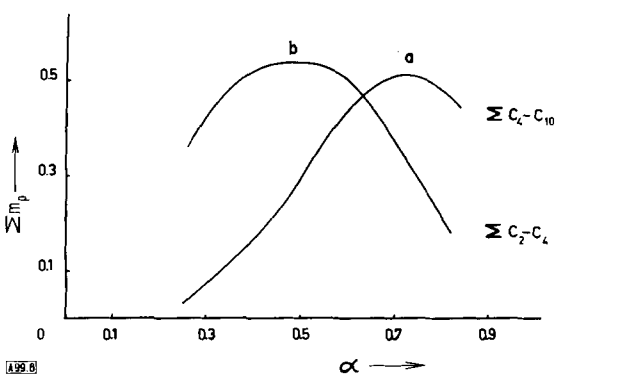


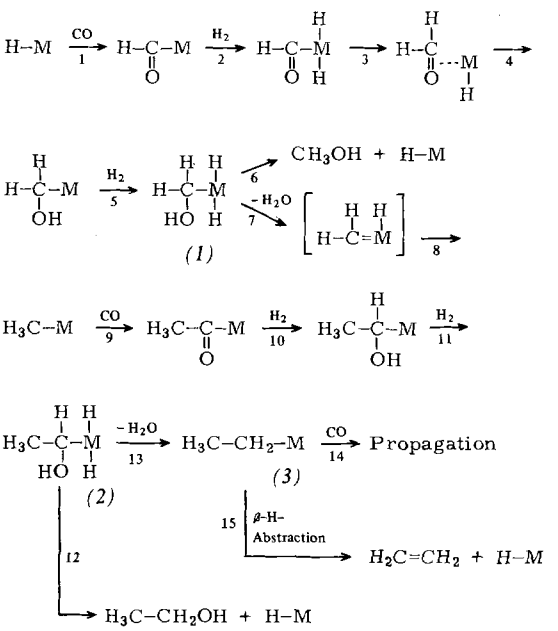
Fig. 6. Weight fractions of different ranges as a function of α, calculated according to Eq. (4).

Since these calculated curves are invariant consequences of the Schulz-Flory molecular weight distribution, future work can now be directed to the search for those experimental conditions (catalyst composition, pressure, temperature, feed gas composition, space velocity, *etc.*), which would give the α value recognized as the most favorable for a desired molecular weight range [cf. Fig. 6 and Eq. (5)].

6. Reaction Mechanism

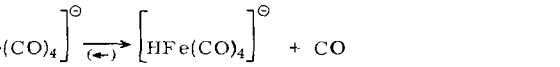
The sum of the information reported in the preceding Sections, and gathered from various sources, prompted us to suggest a unified reaction mechanism for the Fischer-Tropsch synthesis. In formulating such a reaction scheme we follow a contemporary trend, probably first expressed by *Nyholm*[19], of looking at heterogeneous catalysis with transition metals more from the point of view of individual active centers and of their coordination chemistry, than from that of "active surfaces". Therefore we have tried to base the suggested reaction scheme, as far as possible, on individual steps well established in the homogeneous catalysis with soluble transition metal complexes. Such individual steps are, *e.g.*, coordination of CO and of olefins, oxidative addition and reductive elimination, insertion, as well as β-H abstraction (β-H transfer)[20]. The mechanism must also take into account that alcohols as well as α-olefins are primary products; this excludes the former as precursors of the latter.

The suggested mechanism is represented in Scheme 1. The initial metal hydride may be assumed to arise during the activation of the catalyst. Carbon monoxide is coordinated to the metal center and inserted into the M—H bond (step 1)[*]. A hydrogen molecule is oxidatively added to the metal center (step 2). Reductive elimination of the acyl ligand and one of the hydride ligands gives formaldehyde plus a metal hydride (step 3); the former, however, does not leave the metal center, but remains coordinatively bonded through its C=O group (aldehydes are not primary products of the Fischer-Tropsch reaction, cf. Section 3). Addition of the metal hydride to the aldehyde is the next step (step 4), followed by another oxidative addition of H_2 (step 5). Intermediate *(1)* can react in one of two possible ways: reductive elimination (step 6) to give methanol and a metal hydride which can continue the kinetic chain, or elimination of water, with the intermediate formation of a carbenoid ligand (step 7), which rearranges to give σ-bonded methyl ligand (step 8). Now the next CO molecule can be coordinated and inserted (step 9). The next step (step 10) actually summarizes the result of three steps, corresponding to steps 2—4, with the difference that the carbon chain is now increased by one unit. Oxidative addition of H_2 (step 11) leads to the intermediate *(2)* which can again undergo two alternative reactions, giving either the alcohol by reductive elimination (step 12), or the alkyl group by H_2O elimination (step 13, which summarizes the two steps



Scheme 1. Mechanism of the Fischer-Tropsch reaction.

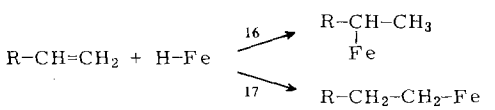
[*] *The insertion of CO into a M—H bond has never been reported.* But the reverse reaction



has been recently investigated [21], indicating that the equilibrium lies far on the right. Nevertheless, kinetically significant amounts of the reaction product of the carbonylation of a metal hydride may well be expected to be present.

corresponding to steps 7 and 8). The alkylmetal compound can either add CO and thus contribute to chain propagation (step 14) or, by β-H transfer, give an α-olefin (ethylene at this stage) and a metal hydride which continues the kinetic chain (step 15).

Presumably, the metal hydride is also responsible for the secondary reactions such as hydrogenation and incorporation of the α-olefins. Coordination and insertion of an α-olefin into a M—H bond can occur in either of two ways:



Step 16 and further growth will lead to monomethyl-branched compounds, whereas step 17 gives a linear prolongation of the previously olefinic chain. This explains why methyl branching is the only significant branching experimentally observed.

At present, this reaction mechanism cannot be more than a working hypothesis which explains, at least qualitatively, most of the experimental findings, without violating known reaction patterns of transition metal centers.

Several questions remain open; *e. g.* why is alcohol formation favored by high pressure and high H_2/CO ratio? Or, why has it not been possible so far to carry out a Fischer-Tropsch synthesis in solution, with a soluble transition metal complex? The answer to the latter question may be related to a general phenomenon in heterogeneous catalysis: solid reduced transition metal catalysts have, on their surfaces, low valent, coordinatively unsaturated metal species which easily offer the sites required for catalysis, whereas in solution coordination of solvent molecules or cluster formation tend to block such sites.

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New analytical methods (5)

Integrated Dust Analysis by Physical Methods

By Hanns Malissa[*]

Environmental analyses show that the air which we breathe, and which is so essential to life, is in general a mixture of gaseous, liquid, and solid components. The solid airborne particles, whose concentration, homogeneity, chemical composition, size, and shape can vary over wide ranges, and whose origin may be "natural" or "artificial" are referred to as "dust". Dust particles can act, *inter alia*, as condensation nuclei, catalysts, and directly as hazardous materials. Unfortunately, we still know far too little about dust. Dust analysis is extremely difficult and challenging, even for modern analytical chemistry; it is still far from being fully automated. The simultaneous determination of as many "dust parameters" as possible, and particularly the synoptic consideration of all available data against a background of physicochemical and technological knowledge on the development, transformation, and effects of dust, are summarized as "integrated dust analysis".

1. Introduction

With the concept "integrated dust analysis" an attempt is made to express the fact that the nature and effects of dust can only be understood if the dust sample is examined as completely as possible *in situ*, and that *one* analytical method alone is not adequate for this purpose.

The present review outlines the significance and performance of integrated dust analysis and then goes on to consider a few general problems of dust analysis.

Most difficulties in the assessment of analytical results stem not only from the sample or the methods employed, but rather from the problem formulated.

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The primary question in the case of dust analysis is: "What is dust and where do the limits of its analysis lie?"

According to *Bibbero* and *Young*[1] dust is defined as solid particles of "any size", *i.e.* airborne particles ranging from 10^{-4} µm (small molecules, large ions) to 10^{3} µm (particles already visible to the naked eye). It is in this range of particle size, which stretches over some seven orders of magnitude and in which inhomogeneities of chemical composition and shape arise due to adhesion and agglomeration, where the main problems of dust analysis lie.

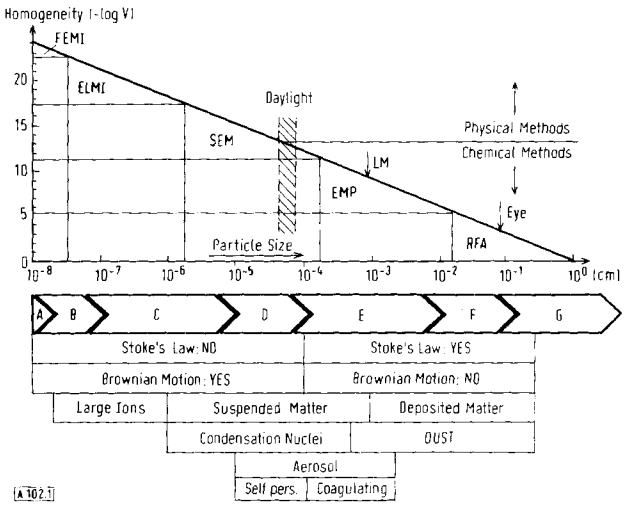


Fig. 1. Particle size in environmental analysis. LM = light microscope, RFA = X-ray fluorescence analysis, EMP = electron microprobe, SEM = scanning electron microscopy, ELMI = electron microscopy, FEMI = field electron microscopy. A: atoms, B: molecules; C: Aitken particles; D: large particles; E: giant particles; F: fine solids; G: coarse solids.

Figure 1 illustrates the interrelations between particle size, physical behavior, and homogeneity. The behavior of the particles (such as motion, adsorption and absorption, or chemical reactions) is determined by the physical and chemical laws that are valid for finely divided material. As a measurement of homogeneity[2] we use the logarithm of the reciprocal of the analytical volume (log $1/V$), which—within a certain standard deviation—yields the same result in measurements on samples taken from various sites as in repeated measurements on one and the same sample. The question of homogeneity is directly related to the degree of resolution of the method of examination employed. For X-ray fluorescence analysis (RFA), particles under 100 µm are in all events homogeneous, whereas if electron probe microanalysis or scanning electron microscopy (SEM) is employed they could be heterogeneous.

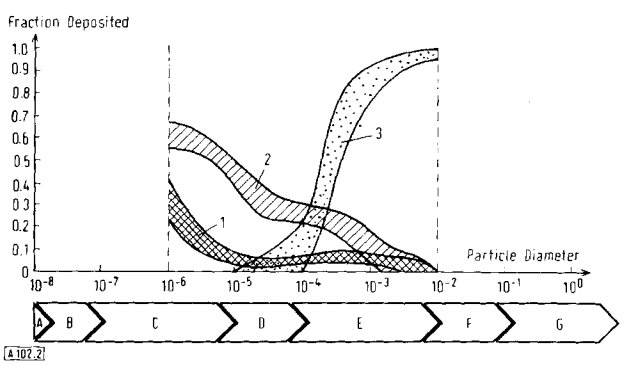


Fig. 2. Deposition of dust according to particle size. 1: tracheobronchial; 2: pulmonary; 3: nasopharyngeal (cf. also Fig. 1).

This means that the RFA method suffices up to homogeneity class 5, the SEM method up to 16. The highest homogeneity would be achieved if every atom in the sample were the same as the rest (homogeneity class 24).

It is already well known that the harmfulness of dust does not depend on the chemical composition alone, but also on the particle size and shape. Recent work by *Natusch* and *Wallace*[3] shows that small particles are generally more dangerous than large ones. The reason for this lies in the processes of breathing and deposition (cf. Fig. 2). Usually the dangerous components such as lead, cadmium, selenium *etc.* are present as small particles. It was found for example that prolonged exposure to coarse grained MnO_2 was not injurous to health, whereas a finer dust of the same substance (80% of the particle diameters <2 µm) caused pneumonitis. The influence of particle shape has so far not been studied in great detail, but one can assume that angular particles are more dangerous than rounded ones. This opens up yet another field for cooperative research (analysts, doctors, *etc.*). Furthermore, it is also known that dust is far from being a homogeneous product—neither from the point of view of particle size or shape, nor from the standpoint of composition. This leads to considerable difficulties in analysis, but can make the investigation of dust a very interesting task. In the analytical sense dust is an agglomerate, the characterization of which demands special consideration of the problems of homogeneity; for its clarification the methods of stereometric analysis are resorted to.

Detailed characterization of dust requires the following analytical steps (where possible, carried out simultaneously):

1. Average analysis of all or individual elements;
2. Identification and quantitative analysis of individual particles of dust;
3. Determination of particle mass (concentration), particle size, and particle-size distribution;
4. Determination of morphology.

Together with stereometric analysis[2] they form the basis of integrated dust analysis. Today the analyst has a wealth of equipment at his disposal for carrying out these determinations, so, in principle, achievement of the aims of such an analysis is not impossible.

2. Sampling

The arsenal of apparatus normally employed for the sampling of airborne dust, which has a particle size of approx. 0.01 to 100 µm, includes filters, dust collectors, electrostatic separators, cyclones, and impactors.

The widely adopted technique of dust sampling with the aid of filters is highly efficient. By using millipore filters with a defined pore-size, dust having a particle size down to 0.1 µm can be trapped with almost 100% efficiency.

Dust collectors are cheap and easy to handle but have the disadvantage that the dust must be separated from rainwater before the analysis. As a side-effect any SO_2 dissolved in the water can react with the dust and thus lead to a change in composition. A further disadvantage is the time required for sampling.

Electrostatic separators are best suited for the collection of smaller dust particles—down to a particle size of 0.01 µm. Cyclones are optimal for the separation of larger particles

(down to 5 μm). Impactors offer the advantage of simultaneous collection and fractionation of particles (working range down to 0.01 μm).

Next to deciding the correct method of sampling, greatest importance attaches to the choice of sampling site. This depends in the first place on the purpose of the investigation: immission or emission measurements. In each case meteorological factors such as wind direction, wind strength, temperature, moisture *etc.* must be taken into consideration.

A further important parameter is the duration of sampling. Each sample collected over a definite period of time yields average data for that interval of time (cf. Fig. 3), *e.g.* the daily average concentration of lead in the atmosphere, if collected over 24 h. If, on the other hand, the sampling time is shortened to 12 h, one obtains not only the daily average value but also the main deviations occurring half-daily. Sampling at three-hourly intervals leads to even more detailed information—for example that the lead concentration is especially high at peak traffic times.

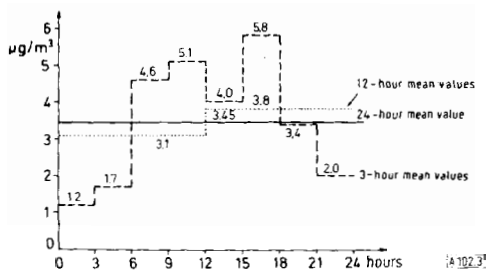


Fig. 3. Dependence of analytical information on duration of sampling. – Example: lead content of air at a street crossing in Vienna (after *Hartl, Müllner, Resch,* and *Wagner*).

Generally speaking, the information content of a sample is the higher, the shorter is the duration of sampling and the more complete is the analysis. The shortest possible duration of sampling is determined by the time required to separate the minimum amount of dust needed for the analysis.

Since the average concentration of dust in towns is about 100 to 50 μg/m³ and since dust can be separated from *ca.* 20–100 m³ of air per hour, the amounts of sample available for analysis lie in the milligram range. This leads to the first unavoidable claim on the technique of analysis to be employed: only micro methods are adequately suitable. If one now considers that a series of physiologically important elements are present in nanogram or microgram quantities in these few milligrams of dust sample we arrive at the second important feature required of the analytical technique: The methods must be highly sensitive, as defined in terms of trace analysis. Summarizing, this means that micro-trace methods are required for dust analysis. Also characteristic of such samples is that dusts are complex multi-element systems and the element to be determined can be present over a wide range of concentration (of % to ppb). Hence the overall analytical problem is "simply" that the analyst must have at his disposal non-destructive multi-element methods for the analysis of microsamples which can cope with a concentration range of about eight orders of magnitude and a particle-size range of about seven orders of magnitude.

If we check the arsenal of modern analytical chemistry with regard to the attributes required, we find that physical micromethods are best suited for dust analysis, since only these comply with the requirements of the sample and the previously formulated problem. The problem cannot however be solved on the basis of a single method.

3. Determination of Average Composition

In integrated dust analysis determination of the average composition is not only important, but essential—and especially for keeping a check on single particle analysis. The most important methods at the moment for the average analysis of a dust are X-ray fluorescence analysis (RFA) and atomic absorption spectroscopy (AAS).

The RFA method can be used for the qualitative and quantitative analysis of all elements having atomic numbers greater than 11 (Na)[4–6]. The practical execution of the analysis using the appropriate standards is simple—usually the filter loaded with dust is analyzed directly (without further treatment) (Fig. 4). Since the depth of signal generation in fluorescence excitation is about 50 μm, filter material is also excited along with the thin layer of dust. The characteristic intensity of the element being measured is directly proportional to the excited amount of element A in dust and filter. The correct intensity of an element in the dust is obtained by subtraction of the intensity of A in a blank filter. Since the surface area analyzed is usually *ca.* 3 cm², then with a signal generation depth of *ca.* 50 μm, a volume of *ca.* 0.02 cm³ will be excited. If the density is 2 g/cm³, then approximately 40 mg of sample of a compact material is analyzed; however, in the case of analysis of dust on filter paper the value is considerably lower.

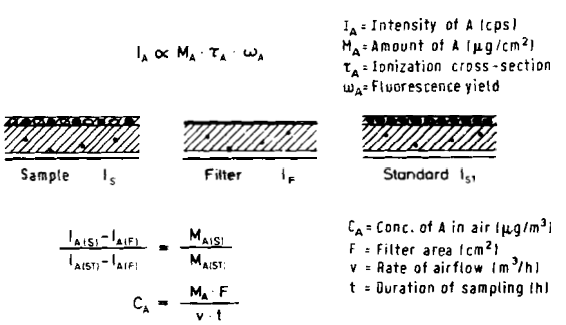


Fig. 4. Quantitative analysis of filter dust with the RFA method.

The quantitative analysis is based on comparison measurements against one or more standards; in most cases these are filters loaded with a definite amount of the element to be determined[7]. The standards are often prepared by spraying a compound on the surface of the filter paper. *Gilfrich et al.*[4] have pointed out the errors that can arise if soluble salts are used as standards instead of insoluble compounds (*e.g.*, for Mg and Al, correction factors of 31 and 20% respectively, are necessary).

It is a matter of conjecture whether this type of standardization really is the best, since the element to be analyzed is often present in different compounds. Thus, *e.g.*, Pb can be bound to oxygen, halide or sulfate. Depending on the chemical shift the band maxima of Pb can lie at different wavelengths. This effect, of course, plays only a subordinate role in RFA, since the resolution in this method is low. However, the effect is relevant in the case of electron probe microanalysis (EMP).

From the ratio of count rates (cf. Fig. 4)

$$\frac{I_{A(S)}-I_{A(F)}}{I_{A(ST)}-I_{A(F)}}$$

one obtains the amount of element deposited. The result is normally given in $\mu g/cm^2$ and converted into the usual concentrations used for hazardous solid materials. The multichannel analyzers presently being used in many industrial establishments have proved very useful for the analysis of dusts; they enable the simultaneous determination of 20 elements in approximately 2 min (in automated operation).

It follows from the direct proportionality between the intensity of a characteristic X-ray line and the fluorescence yield, that elements of the 2nd period cannot be determined with sufficient sensitivity by the RFA method because ω_A drops below 1% at such low atomic numbers.

Excitation with electrons in the macroprobe is useful for the quantitative analysis of these elements, especially C and O, since the decrease in fluorescence is compensated by a corresponding increase in ionization cross-section on account of the different mechanism of signal generation.

As example, we might mention here the determination of the C content of street dust with the macroprobe[8]. In the analysis of samples of street dust collected during a survey in Vienna (Fig. 5), which was concerned with the local and yearly change of concentration of nine elements, carbon contents of 2.7 to 9.2% were routinely determined. The dust sample collected in April, with a value of 7.7% (average value of all 26 collection points), shows the highest proportion of carbon. This can be ascribed to domestic heating systems which give rise to considerable emission of soot. In summer the C-values are around 25% lower.

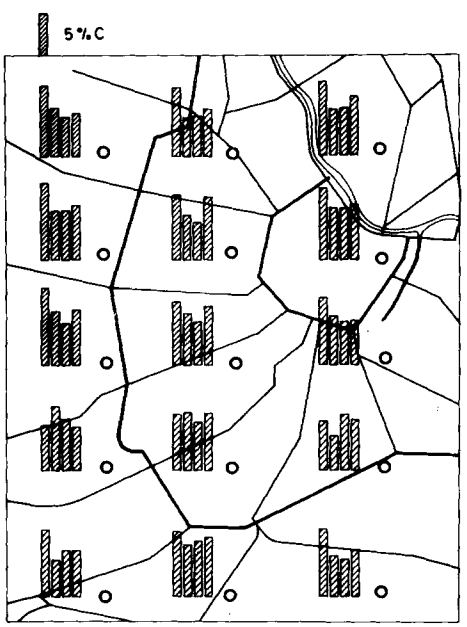


Fig. 5. Dust cadastre of Vienna: Carbon content of street dust [8].

A further disadvantage of RFA (but in this case seemingly slight disadvantage in comparison to the advantages) is the dependence of the signal intensity of an element on the particle size of the dust. At particle diameters of more than 5 μm, intensity losses of 50 to 90% can occur. The reason for this is that the absorption of the characteristic radiation in larger particles is stronger than in smaller ones.

Since the particle size distribution is usually unknown, corrections for this effect can rarely be made. Thus, the accuracy of dust analyses by the RFA method lies in the region of *ca.* ±20%. Though this is perfectly satisfactory in the majority of analyses, in individual cases a higher accuracy—if possible still with the same sensitivity—is desired. Atomic absorption spectrometry (AAS) would be suitable for such analyses[9,10].

At present, AAS provides good results only for liquid samples. This means that the dust sample must be dissolved—either partially (*e.g.* with HNO_3/HCl) or completely (*e.g.* with HF/HNO_3 under pressure in a teflon bomb or with $LiBO_2$)[11]. About 0.5 to 1 mg of sample is required for the determination of an element. The individual elements can so far be analyzed only sequentially, but with great accuracy.

Each chemical workup of the dust has the disadvantage that, on the one hand contamination with impurities can occur, and, on the other, that the bonding of the elements can no longer be determined; moreover, dilution of the system takes place. Because of this dilution—100 mg of dust becomes 100 ml of solution, *i.e.* a dilution of the order of 10^3—AAS, though in itself a sensitive method, does not usually show a higher sensitivity than RFA on evaporation of the sample in a flame.

Table 1 compares the sensitivities of the determination of Cu, Zn, and Pb by various methods. The limits of detection are based on the content of the element in the dust. It can be seen that the detection limit of AAS, the method usually employed, is poorer with flame evaporation than that of RFA, but the precision is better.

Table 1. Sensitivity of the determination of Cu, Zn, and Pb in dust (calculated according to Refs. [4, 6, 12]).

Method	Amount of sample	Limit of detection [a] [ppm]			Precision and reproducibility [% rel.]
		Cu	Zn	Pb	
RFA	1 mg/cm²	10	10	50	≈20
AAS (flame)	1 mg/ml	50	10	200	≈ 1–5
AAS (Graphite tube cuvette)	1 mg/ml	0.05	0.01	0.1	≈10–30
Optical emission spectroscopy	20 mg	10	10	1	≈10–100

[a] Based on concentration in the dust.

The sensitivity of AAS can be increased either by chemical enrichment of the trace metals in the sample solution or by use of the graphite tube cuvette. In the case of the elements quoted an increase in sensitivity by a factor of about 10^3 is possible with the graphite tube cuvette; however, the accuracy of the determination decreases to *ca.* ±30% rel. (after *Coleman*[12]). The most recent development of employing so-called plasma torches and incorporating gratings on a Rowland circle is receiving a great deal of attention, since it will probably enable the simultaneous flame-photometric determination of several elements in very low concentrations.

In some cases (*e.g.* Pb) better limits of detection are achievable with optical emission spectroscopy, since this is also a method in which the sample is excited directly without

dilution. However, the results can often be regarded as only semiquantitative.

Table 2. Quantitative investigation of a fly ash by X-ray fluorescence analysis (RFA) and atomic absorption spectroscopy (AAS) [4].

Element	RFA [μg/cm²]	AAS [μg/cm²]
S	3.2	
K	3.5	
Ca	0.30	
Fe	0.30	0.28
Ni	0.40	0.008
Cu	0.80	0.11
Zn	13	11
Cd		0.097
Pb	4.4	4.8

Table 2 shows the efficiency of RFA and of AAS in dust analysis using the results obtained for a sample of fly ash. The main elements, which are present in the ng or μg range, can be determined with RFA and/or AAS. Generally speaking the results can be said to be in good agreement. Large differences can be attributed to lack of sample homogeneity. In this connection it must be pointed out that precision and reproducibility in the analysis of dusts are also influenced, to a not inconsiderable amount, by the statistical error—*i.e.* by the small number of dust particles to be analyzed. This statistical error can be conveniently calculated with the aid of a formula described by *Wilson*[13], which, to a first approximation, states that the statistical error is $100/\sqrt{N_A}$, *i.e.* inversely proportional to the square root of the number of particles analyzed. Thus, in the analysis of Cu, one has to reckon with a statistical error of ±30% rel. (RFA) for a Cu content of 10 ppm, assuming a particle size of 5 μm. Of particular interest among the numerous new developments in AAS are the variants with microwave-plasma torches and multichannel grating spectrometers, since the amount of sample required is small and an automatic, simultaneous determination of up to 64 elements is possible.

Other methods used for carrying out average analyses of highest sensitivity are spark-emission mass spectrometry and neutron activation analysis. In comparison with the previously described methods they have considerable disadvantages—such as highly expensive apparatus, long analysis times, low accuracy *etc.*—and consequently find little application.

4. Analysis of Single Dust Particles

The most suitable method for the identification of dust components is the elemental analysis of single dust particles. Since airborne dust has a particle size range of *ca.* 100 to 0.01 μm the electron microprobe can be used for the analysis of single particles. The volume of sample excited by the fine-focused electron beam in point measurements is only a few μm^3 and thus makes a selective analysis of single particles possible. Sample preparation is simple: the filter dusts employed in RFA measurements can be analyzed directly after they have been coated with a thin layer of electrically conducting carbon by evaporation; loose dusts, such as are obtained in other dust collecting methods are transferred to a teflon platelet coated with adhesive carbon conductivity paste. Figure 6 shows a typical example of a dust analysis

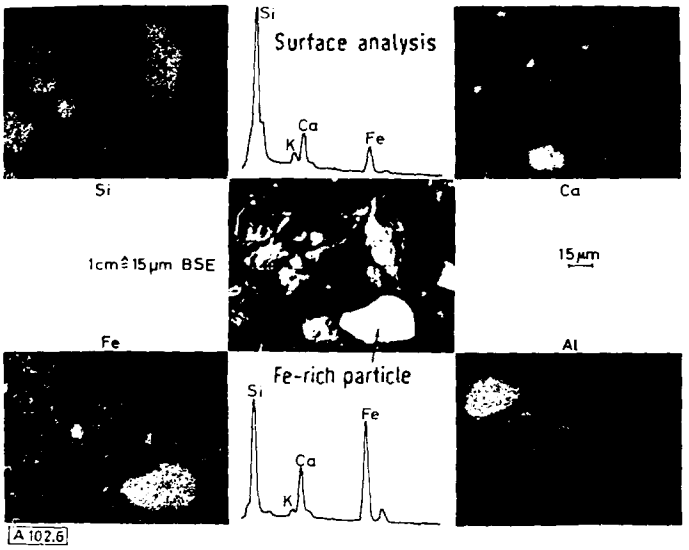


Fig. 6. Electron microprobe analysis of airborne particles.

with the microprobe. The electron back-scatter picture (center) not only gives information about the average atomic number, but also about the shape of the single particle. The energy-dispersion X-ray spectrum (upper right, center) yields semi-quantitative information about the concentration of the elements having atomic numbers greater than 11 (Na) that are present in the area scanned. This result might also serve as guide for any subsequent AAS investigation, in that suitable lamps and preparative steps can be carefully selected. The distribution of the elements can be plotted as the element-specific X-ray signals; the distribution pictures make it possible to give semi-quantitative information about the elemental composition of individual particles—thus, that the particle on the upper left, for example, is an aluminum silicate. The next task consists in quantitatively analyzing a single particle by point counting. The energy-dispersive X-ray spectrometer is well suited for the analysis of rough surfaces, since all elements at the same angle are measured. Crystal spectrometers must be employed for the determination of elements of the 2nd period. In binary systems, quantitative analysis is achieved

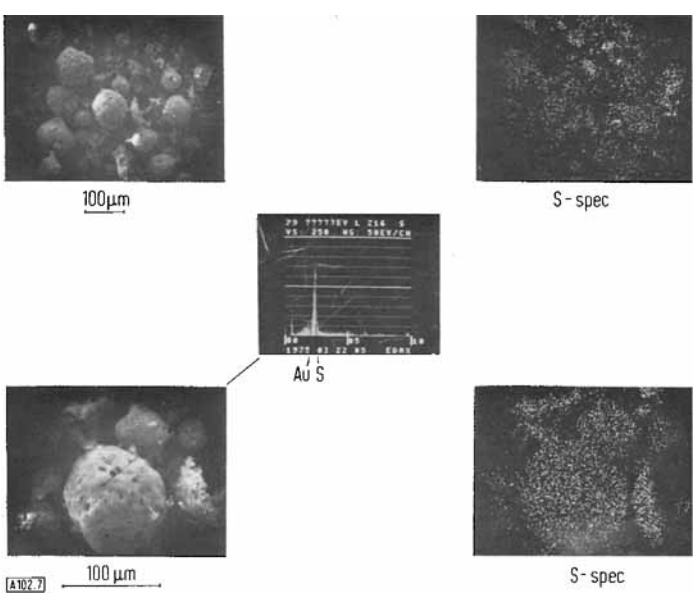


Fig. 7. Scanning electron microscopy of a dust particle collected in the vicinity of a district heating plant with energy dispersive X-ray analysis.

by evaluation of the counting rates and comparison with the corresponding data for standards containing the elements under consideration, since this quantity is largely independent of surface roughness and particle size—*i.e.* it still applies to particles that are smaller than the volume excited. Because of the roughness of the particle surface the achievable accuracy of the analysis is less than in polished samples, and lies in favorable cases at about 5–20% rel. This, however, is satisfactory in most cases.

The application of this technique and wavelength dispersion analysis can afford a wealth of information. Figure 7 shows electron back-scatter pictures (left) of single dust particles. The presence of sulfur was determined by recording an energy dispersive X-ray spectrum (center) and its distribution plotted with the wavelength dispersive spectrometer (right). In order to obtain more information about the sulfur compounds present, a temperature differentiated relative conductometric S and C analysis was carried out (cf. Fig. 8a)[14]. This method yields specific and typical degassing curves for carbon and for sulfur compounds.

Figure 8 shows that the degassing or combustion of such components can be very different, depending on the dust. In the dust of the first example, which contains 60.6% C and 10.9% S, loss of sulfur begins at 270°C. 20% of the total content is lost below 500°C, then a further 40% up to 600°C. In the interval to 1000°C the sample slowly loses another 20% of sulfur, and finally the rest in the interval up to 1200°C. In contrast, the volatilization of carbon proceeds very much differently. It is entirely lost within 200° at relatively low temperature.

Investigation of a dust, which was collected at the same time at another site by the Bergerhoff method, and which also proved to contain similar spherules (Fig. 9) but in smaller proportion gave total carbon and total sulfur contents of 8.4% and 1.8%, respectively. The degassing curves (Fig. 8b) are markedly different. 80% of the sulfur in this second example is volatile only above 1100°C. Loss of carbon is retarded and shows a significant step at 600°C for a residue of *ca.* 20%. From volatility curves the presence of "organic" and "inorganic" carbon as well as sulfur can be concluded. Thermal decomposition of $CaSO_4$ takes place between 1100 and 1300°C. The decomposition of $CaCO_3$ begins at 825°C, that of $MgCO_3$ at 325°C.

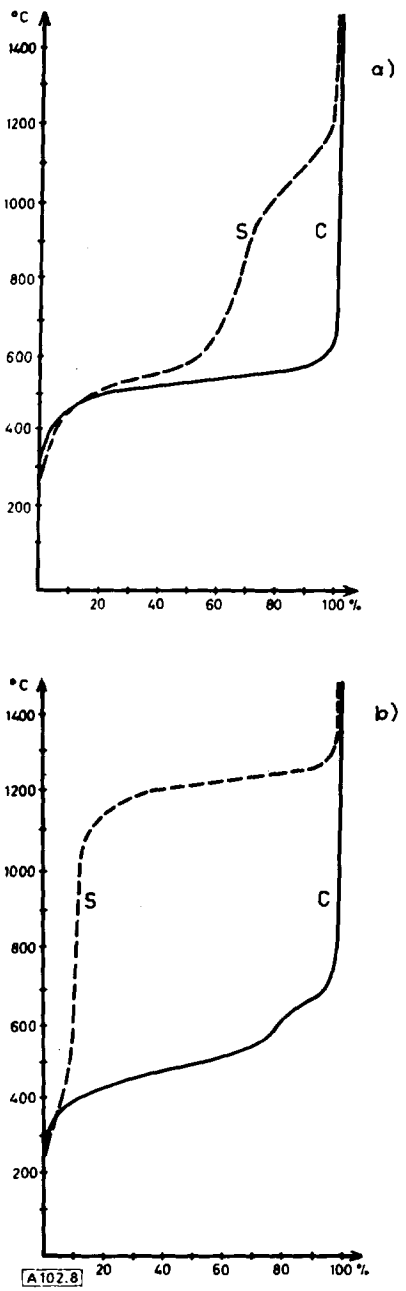


Fig. 8. Relative conductometric carbon and sulfur analysis with a temperature program: a) dust with 60.6% C and 10.9% S (cf. Fig. 7); b) dust with 8.4% C and 1.8% S (cf. Fig. 9).

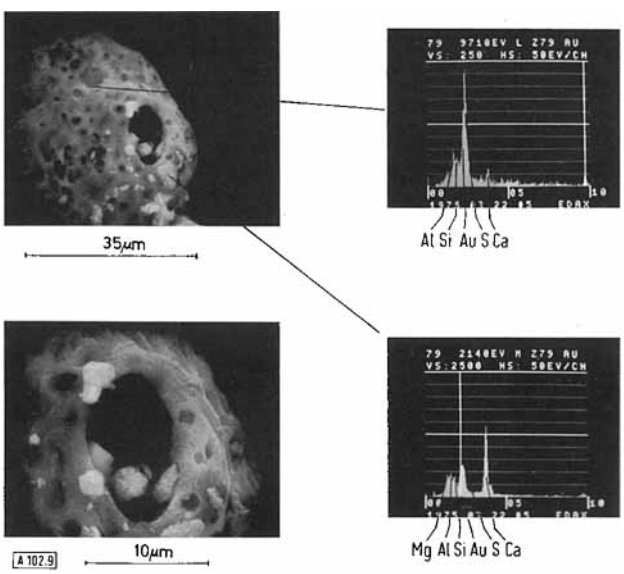


Fig. 9. SEM picture and energy dispersive X-ray analysis of a dust particle collected in a city.

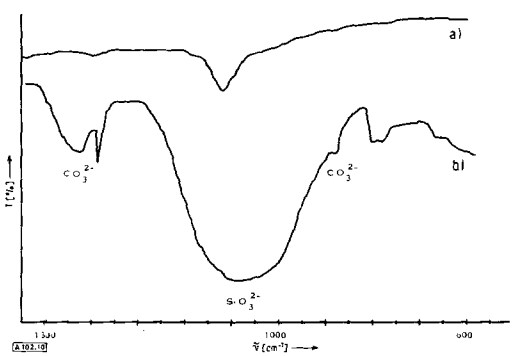


Fig. 10. IR spectra of, a) soot (cf. Fig. 7), and b) street dust (cf. Fig. 9).

In the IR spectrum of another fraction of this sample two bands are observed which can be assigned to the carbonate (Fig. 10b). Further investigations are called for in this obviously productive sector.

From the electron microprobe analysis (EMP) of the dust particles referred to in Figure 9 it follows that relatively large carbon particles are accompanied in this case by many small (1–5 μm) particles of other composition. The spectrum of the small particles shows that they contain more Mg and Ca and less Al and Si. Such particles are even found in the centers of the carbon particles. It is to be assumed that all particles can exhibit various effects and take on all sorts of attitudes.

In a modified analytical method the dust particles are inbedded in a resin; after polishing, the accuracy of the quantitative elemental analysis for particle sizes above 10 μm is improved to 1–2% rel. Using this method *Pietzner* and *Schiffers*[15] were able to identify the particles in waste gas from coal firing. In this connection the particle atlas by *McCrone et al.*[16] is very useful.

The ESCA method, which was introduced by *Siegbahn et al.*[17] and whose use in dust analysis has been particularly well demonstrated by *Novakov*[18], affords additional information. Thus, for example, it could be shown experimentally that soot plays an important role in the catalytic oxidation of SO_2 to SO_3 in the atmosphere. Auger spectroscopy likewise affords further information about chemical bonding. It ought to be utilized more than hitherto for research into the reactions between gaseous and solid substances polluting the atmosphere. Auger transitions as well as autoionizations can be excited by X-rays and by electron bombardment. Basic knowledge has already been gained with studies on CO[17].

In many cases it is not possible to arrive at an unequivocal clarification by elemental analysis, especially if several compounds differ only very slightly in their composition (*e.g.* PbO, PbO_2, and Pb_3O_4 or some silicates). The elemental information obtained with the microprobe must then be supplemented with compound-specific information—*e.g.* from valence band spectroscopy[19]. As can be seen from Figure 11, using the oxygen-K bands of Fe_2O_3 and $Fe_2(SO_4)_3$, the valence band spectra of an element in various compounds show clear differences in band position, width, shape and intensity ratios. These differences can serve for the identification of compounds.

In the case of the lead-oxygen compounds (Fig. 12) the intensity ratios between satellites and main band in the oxygen spectrum, their half-width, and asymmetric number are typical for a definite compound. This permitted characterization of the lead-containing dust particle shown in Figure 13.

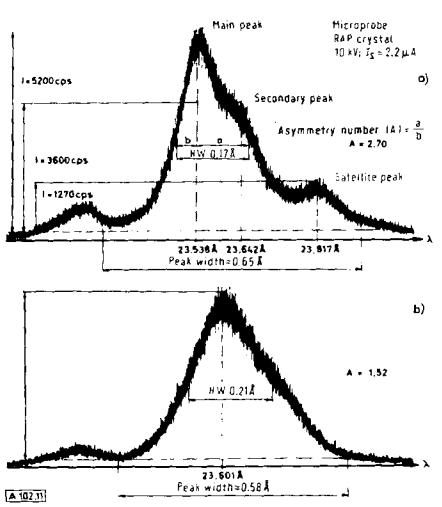


Fig. 11. Oxygen valence band spectrum of, a) $Fe_2(SO_4)_3$ and b) Fe_2O_3 [19].

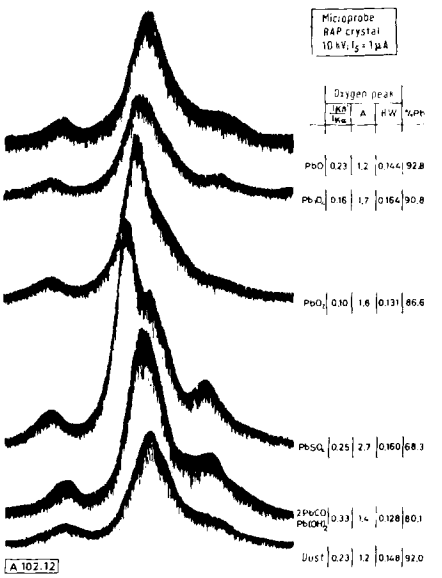
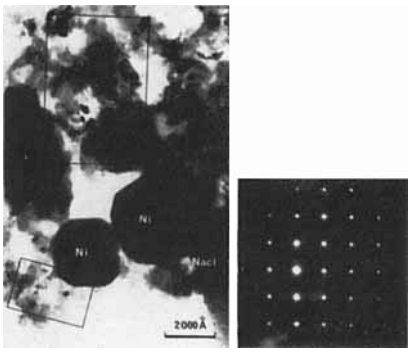


Fig. 12. Oxygen valence band spectra of some lead compounds [19].

Fig. 13. a) Back-scattered electron picture and b) lead distribution of dust (1 cm = 60 μm).

X-Ray diffraction is also suitable for the identification of compounds occurring in a dust sample, particularly if preliminary data—*e.g.* average elemental analysis and composition of individual dust components—are available. This method was used by *Rickards*[20] for the determination of asbestos in dust and for differentiation of the various types of asbestos. The application of X-ray diffraction for the identification of compounds has the disadvantage, however, that the evaluation of multielement systems is tedious and the method insensitive. The limit of detection lies at 1–10 wt% of the compound in the sample. This constitutes a particular disadvantage if the particle size of the dust component sought is less than 1 μm, since an identification on the basis of elemental analysis with the microprobe is then impossible.

For particle sizes below 1 μm there is still the possibility of identifying the compounds contained in a single particle by recording an electron diffraction diagram[21]. Particles down to 100 Å diameter can be identified in this way—provided preliminary supporting data are available, *e.g.* on the qualitative elemental analysis, obtainable in one operation with a modern scanning transmission electron microscope (Fig. 14).



A 102.14 a) b)

Fig. 14. a) SEM micrograph of a nickel ore, roasted with NaCl; b) electron diffraction diagram of a NaCl particle.

Thus, in investigations on fluorine-containing airborne particles, *Radczewski*[22] was able to differentiate between the naturally occurring cubic K_2SiF_6 and the hexagonal K_2SiF_6, formed in industrial processes. This finding provides an important indication to the origin of the fluoride contamination.

Another technique employed in the identification of small particles is the evaluation of energy-loss spectra of the transmitted electrons in a scanning transmission electron microscope. Figure 15 shows a sample of MgO particles and their energy-loss spectra. Discrete bands in the continuum correspond to discrete energy-loss by the electrons in the ionization of an atom. The $MgL_{2,3}$ bands arise from the ionization of the magnesium $2p_{1/2}$ and $2p_{3/2}$ orbitals. A qualitative analysis would appear to be possible by determination of the ionization energies. The lateral resolution of this method is *ca.* 100 Å.

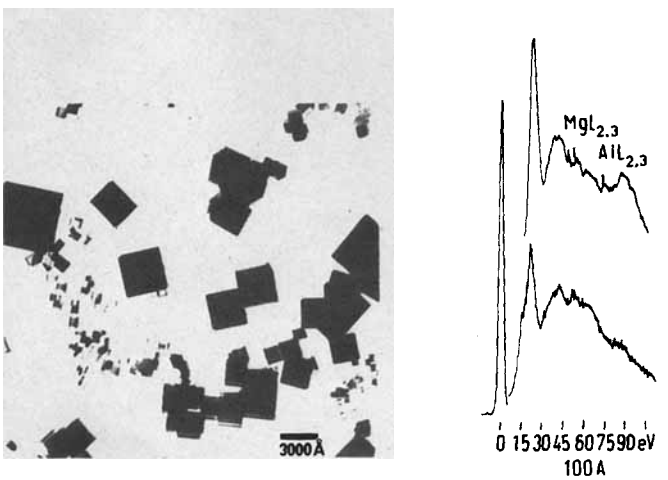


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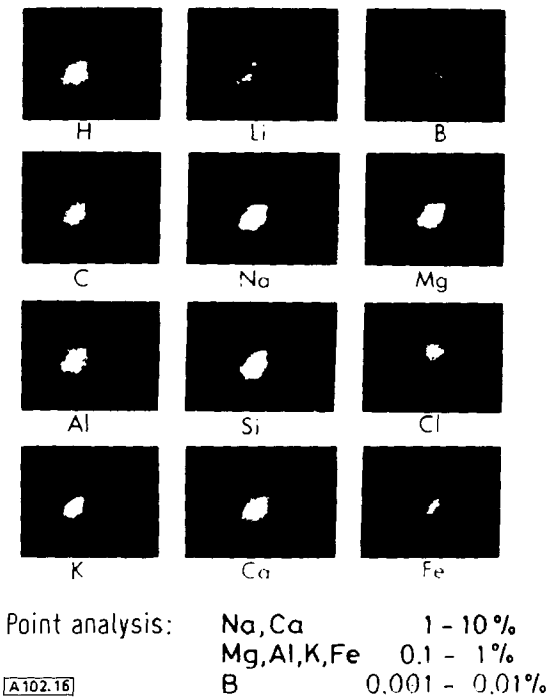
Fig. 15. Energy-loss spectrum of MgO particles on an evaporated Al layer.

A further limitation to the use of the microprobe arises from the relative insensitivity of the EMP method: the detection limit lies at a concentration of *ca.* 0.1%, with an excited volume of a few μm^3; this means that trace components of a single dust particle cannot be detected, even though the microprobe permits very low absolute detection limits (*ca.* 10^{-5} g).

As an extension to electron microprobe analysis, a further possibility is ion microprobe analysis, which, because of the higher effective cross-section of signal generation and lack of background interference, has a sensitivity that is higher by a factor of 10^2 to 10^5.

As with the electron microprobe the distribution of the elements to be found in the dust particles can also be recorded with the ion microprobe using the scanning technique, the distribution in this case being isotope-specific. Figure 16 shows as example the ion microprobe analysis of an approx. 8 μm particle of lampback. The main advantage here is that elements whose local concentration lies in the 0.001% range—as in the case of B in this instance—as well as elements of very low atomic number are still detectable. In the local analysis of the dust particle illustrated in Figure 16, *McHugh* and



A 102.16

Fig. 16. Ion microprobe analysis of an oil soot particle [23].

Stevens[23] were able to determine semi-quantitatively 21 elements in the concentration range from 10 ppm to more than 10%.

The great importance of local trace analysis is that the particle's content of trace elements often depends in a characteristic way on the emitters. Thus, *Anderson*[24] was able to identify the emitters by determing the Be content of asbestos fibers (ppm) in dust.

5. Morphology

In addition to the average analysis and single particle analysis of a dust, the determination of the morphology of the particles is frequently also very informative.

The morphology of the dust particles—*i.e.* size, shape, and surface characteristics—is of great importance from the physiological standpoint. Thus, the possibility of penetration of dust into the lungs depends on the particle size (cf. Section 1). Of the physiological effects of shape, it is known that pointed, rigid fibrous particles (*e.g.* asbestos fibers) are especially dangerous. The surface properties are decisive for the dust's ability to adsorb volatile noxious substances and thus evoke synergistic effects.

The investigation of dust morphology requires the use of the light microscope (lower limit *ca.* 1 μm particle diameters[16]) and the scanning electron microscope (lower limit *ca.* 100 Å particle diameters). SEM pictures (cf. Fig. 17) are by far the most informative[11] because higher resolutions and much sharper definitions are possible.

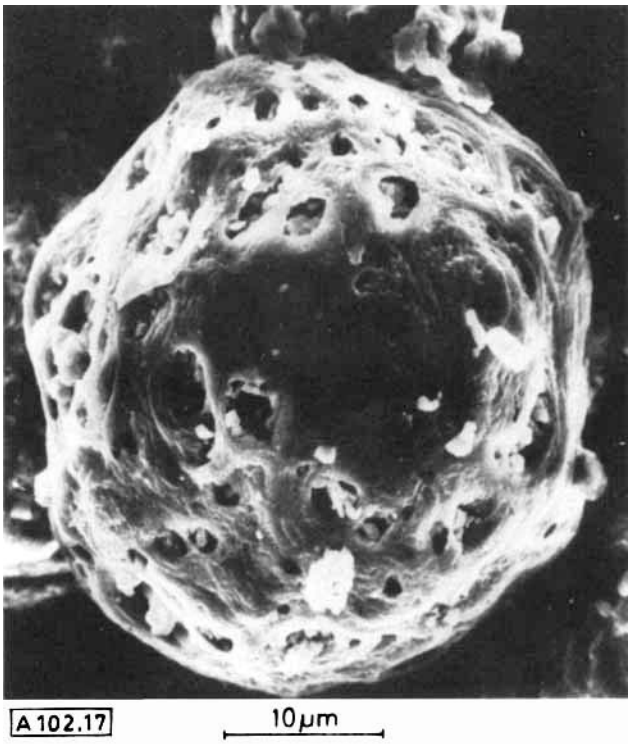


Fig. 17. SEM picture of an oil soot particle (magnification 2000 ×).

Special advantages are offered by an energy dispersion spectrometer fitted with a scanning transmission electron microscope, since such an apparatus enables the analysis of single particles, the determination of crystal structures by recording electron diffraction diagrams, and the morphological investigation to be carried out in one operation.

6. Conclusions

Integrated dust analysis, a novel analytical strategy in which physical, chemical, geometrical, and mathematical operations are combined, provides a wealth of very detailed data. It is still in the early stages of development, but rapid progress is expected in this sector over the next few years. The whole field of dust analysis must be re-examined and the methods of sampling, the possibilities of stereometric investigation of a sample by point, linear, and area analysis with new equipment (*e.g.* phase integrator) brought into line with new concepts and methods of interpretation.

The main analytical points are:

- the chemical composition of the region of sample examined;
- the qualitative and quantitative analysis of single particles;
- the total number of all selected particles;
- the particle size and particle-size distribution;
- the morphology.

The synoptic consideration of the results and the chemical and mathematical evaluation of the data will lead to the desired information.

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Application of Catalyzed Reactions in Analytical Chemistry

New analytical methods (6)

By Herbert Weisz[*]

Catalyzed reactions are becoming increasingly important in analytical chemistry, and especially in trace analysis. The acceleration of a particular reaction (indicator reaction) promoted by the catalyst provides information about the catalyst concentration. Substances which lower or raise the activity of a catalyst (inhibitors or activators, respectively) can likewise be determined in this way. The course of a reaction is usually monitored by physical measuring techniques. Various methods of conducting these kinetic-catalytic studies are discussed in this article.—Use of catalyzed reactions for end point detection in volumetric analysis is also feasible.

1. Introduction

Whenever a definite relationship exists between the extent of a physical phenomenon and the amount of substance giving rise to this phenomenon, measurement of this property can be employed for quantitative determination of that substance. All measurable properties can be utilized for this purpose. During the measurement, the system must be in a state of sufficient stability, *i.e.* in thermodynamic equilibrium.

On the other hand, precisely the change of a property of a system with time may be monitored, *i.e.* time may be employed as an additional measured quantity.

Kinetic analytical techniques of this kind have found increasing application in recent years. Detailed accounts are to be found in the monographs by *Frost* and *Pearson*[1] and *Mark* and *Rechnitz*[2], and especially on practical analytical aspects in the book by *Yatsimirskii*[3]; some more recent surveys should also be mentioned[4–6].

An important group of kinetic analytical methods is based on the use of catalyzed reactions.

These techniques attract particular interest in analytical chemistry, doubtless because they provide a highly sensitive means of detection or quantitative determination of the catalyst itself.

Catalysts are substances which increase the rate of a chemical reaction. The requisite lowering of the activation energy proceeds in such a way that the catalyst is regenerated and thus maintains a constant concentration in the system; hence even small amounts of catalyst can effect high conversions, thus accounting for the high sensitivity of catalytic-kinetic methods.

Catalytic reactions have long held a firm place in qualitative analysis. Mention need only be made of the extremely sensitive iodine-azide reaction for the detection of sulfide[7]; iodine and sodium azide practically fail to react with each other, reaction occurring only on addition of sulfide (or various other compounds of divalent sulfur):

$$I_2 + 2N_3^- \xrightarrow{S^{2-}} 2I^- + 3N_2$$

It is readily observed, both by the disappearance of the brown color of the iodine and by the development of gas bubbles (nitrogen).

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Analytical methods based on the use of catalyzed reactions are of great importance in present-day trace analysis, primarily owing to their frequently marked selectivity (especially in enzymatic analytical methods) and their high sensitivity, comparable with those of activation analysis.

Let us consider the reaction of two substances accelerated by a catalyst K

$$A + B \xrightarrow{K} X + Y$$

The concentration of K can be determined from the extent of this acceleration. The procedure adopted entails monitoring the rate of reaction between the substances A and B for a change in concentration of one of the starting materials (A or B) or of one of the reaction products (X or Y).

The reaction employed for determination (or detection) of the catalyst is called an indicator reaction. That substance whose change in concentration serves as a measure of the progress of the reaction is termed an indicator substance. It may be either a reactant (A or B, iodine in the case of the iodine-azide reaction) or a product (X or Y, elemental nitrogen in the case of the iodine-azide reaction).

The progress of the indicator reaction can therefore be followed by monitoring the depletion of a reactant or the accumulation of a product.

Assuming the indicator reaction to obey the following rate law:

$$\frac{dC_x}{dt} = kC_K C_A C_B \qquad (1)$$

k = rate constant; C_A, C_B = concentration of reactant A and B respectively at a time t

then the reaction is of second order since the catalyst concentration of C_K remains unchanged.

Now if one of the reactants, say B, is present in such excess that its concentration can also be regarded as constant, then we have a reaction of pseudo-first order:

$$\frac{dC_x}{dt} = kC_B^0 C_K C_A = k'C_K C_A = k'C_K(C_A^0 - C_X) \qquad (2)$$

C_A^0, C_B^0 = concentration of A and B, respectively, at time $t = 0$
$k' = kC_B^0$

If it is possible to determine even very small amounts of the indicator substance X by a sufficiently sensitive method of measurement (a small depletion of A is much more difficult

to determine) then determination of the reaction rate can be restricted to the initial state of the reaction. This means that during this brief period the concentration of reactant A can also be viewed as constant and we have a reaction of pseudo-zero order:

$$\frac{dC_X}{dt} \approx k' C_K C_A^0 = k'' C_K = \text{constant} \quad (k'' = k' C_A^0) \tag{3}$$

We see that in the initial state the reaction rate is directly proportional to the catalyst concentration C_K. Integration of this relation affords:

$$C_X \approx k'' C_K t \tag{4}$$

Equations (3) and (4) are the basis of the so-called differential methods. Three basic methods are available for determining the catalyst:

1) Tangent method: the change in concentration of X (C_X) is continuously observed and registered *versus* time. The slope of the resulting straight line, $\tan\alpha$, is a measure of the catalyst concentration (C_K). In the calibration graph the $\tan\alpha$ values are plotted against the corresponding catalyst concentrations.

2) Fixed time method: the amount of reaction product X formed within a fixed, predetermined time interval from the start of the indicator reaction is determined. In the calibration graph the C_X values are plotted against the corresponding catalyst concentrations C_K.

3) Fixed concentration or variable time method: the time which elapses from the start of the reaction until C_X has attained a certain predetermined value is measured. The reciprocal of this time plotted against the pertinent catalyst concentration affords the calibration graph.

If measurements have to be extended beyond the initial state, *i.e.* if the concentration of the reactant A present in lower concentration can no longer be regarded as constant (after consumption of more than 10% of A), then integral methods are used instead of differential ones. They are based on the integrated form of the differential rate law [cf. eq. (2)]:

$$\ln \frac{C_A^0}{C_A^0 - C_X} = k' C_K t$$

There is no longer a linear relation between C_X and t [as in eq. (4)] but a logarithmic one instead. Nevertheless, the three basic methods just described can still be employed.

By suitable choice of reaction conditions (concentration, pH value, temperature, ionic strength) the order of reaction can be modified in such a way that a simple, optimally linear, relation exists between the catalyst concentration and the reaction rate. Most of the indicator reactions used in analytical practice are modified so that they approximately correspond to the above conditions of a pseudo-first order reaction. (Theoretical aspects receive detailed treatment in the monographs[1-3].)

The most frequently used technique for determining the catalytic activity of a sample is the following: The two reactants of the indicator reaction (one generally in great excess) are brought together and the reaction initiated by admixture of the catalyst to the determined. In some cases it is more convenient to first mix one reactant with the catalyst and then start the reaction with the aid of the second reactant; this procedure is recommended above all when the contribution of the uncatalyzed reaction cannot be neglected.

The course of reaction can be followed by chemical or physical methods.

The chemical approach is practicable only in the fixed time method: the reaction is stopped after a suitably chosen time; this can be achieved by rapid cooling or a drastic pH change or, most frequently, by addition of an inhibitor which has a sufficient "braking" effect on the catalytic activity. Then either the unconsumed component of the reactant serving as indicator substance or the product formed since the start of reaction can be determined chemically (generally by volumetric analysis).

Measurement by physical techniques can be applied to all three methods—tangent method, fixed time method, fixed concentration method. This approach entails measurement of the change in some physical property of the system which is proportional to the change in concentration of the indicator substance concerned.

In most of the examples given in the literature, the reaction rate is determined by photometry in the reaction vessel itself which serves as a measuring cell in the spectrophotometer.

Other frequently used methods include highly sensitive fluorescence measurements, potentiometry, biamperometry, conductometry, and, especially recently, enthalpimetric monitoring of the reaction course by thermometric methods; the last method is particularly versatile, thanks to the sensitive thermistors nowadays available.

Since the reaction rate is extremely dependent on temperature (cf. Arrhenius equation) the reaction vessel must always be well thermostated; the enthalpimetric method clearly represents an exception where, by way of contrast, adiabatic reaction conditions must be employed (*e.g.* in Dewar vessels).

The results are usually evaluated by graphical extrapolation from a calibration graph.

Now not only the catalysts themselves can be determined by these kinetic methods but, indirectly, any substance which may influence catalytic activity: inhibitors, activators, reactivators.

Inhibitors, which lower the activity of a catalyst (*e.g.* by precipitation or complexation), are determined by adding the inhibitor to a known amount of catalyst and establishing the fall in the reaction rate by one of the above methods.

A fitting example is the determination of nanogram quantities of mercury by inhibition of the iodide-catalyzed cerium-arsenic reaction[8] (see Section 2.1) (1 ng = 10^{-9} g).

Reactivators (sometimes called pseudoactivators) can reactivate, *i.e.* liberate (*e.g.* by demasking), a catalyst present in an inactive inhibited form (*e.g.* as a complex); measurement of the activity of the reactivated catalyst affords a means of analytically determining such substances: manganese(II) catalyzes the oxidative decoloration of alizarin S by hydrogen peroxide; *trans*-1,2-diaminocyclohexane-*N*,*N*,*N*',*N*'-tetraacetic acid inhibits the manganese catalyst by complexation. Now since lead is able to displace manganese from this complex—and thus regenerate its catalytic activity—microgram quantities of lead can be determined indirectly by this method[8] (1 µg = 10^{-6} g).

Activators enhance the activity of a catalyst and therefore become accessible to determination. For instance, arsenic(III) enhances the catalytic action of osmium on the reaction

between bromate and iodide and has been determined in this way[9].

In principle, a reactant of a catalyzed reaction can also be determined—albeit with a predictably lower sensitivity. This possibility is only employed in enzymatic analyses ("determination of substrate").

2. Indicator Reactions

The reactions used for determining catalytic activity must satisfy a number of conditions:

The extent of uncatalyzed reaction should be as low as possible (ideally zero).

The course of reaction should be easy to monitor, wherever possible by several methods (*e.g.* photometry, potentiometry, thermometry).

The catalyzed reaction should not be too fast, but, for practical reasons, not too slow either; if it is too fast ($t_{1/2} < 10$ s) the time required for thorough mixing of reactants can no longer be neglected.

Hitherto redox reactions and enzyme reactions have been employed most widely as indicator reactions. In addition, limited use has also been made of homogeneous catalyzed exchange reactions of complexes with mono- and multi-dentate ligands.

Concerning the heterogeneous catalyzed electrode reactions already described by *Heyrovsky*[10] (catalytic "waves" in polarography) the reader is referred to the literature.

2.1. Redox Reactions

The principal oxidizing agents used are: hydrogen peroxide, peroxoborate, oxygen, oxoanions such as bromate, iodate, nitrate, peroxosulfate, periodate; the reducing agents include iodide, thiosulfate, arsenate(III), a series of organic dyes such as alizarin, malachite green, azo dyes (*e.g.* methyl orange), other organic substances such as hydroquinone, α-naphthylamine, *p*-phenetidine, *o*-tolidine.

Catalysts that can be directly determined by these reactions include: copper, iron, manganese, titanium, zirconium(IV), thorium(IV), molybdenum(VI), tungsten(VI). Redox reactions catalyzed by osmium and ruthenium have been studied particularly thoroughly.

Other redox systems have also been employed for kinetic determination of catalysts, for example the cerium-arsenic reaction proposed as long ago as 1934 by *Sandell* and *Kolthoff*[11]; it is catalyzed by iodide and by osmium:

$$2Ce^{IV} + As^{III} \xrightarrow[Os]{I^-} 2Ce^{III} + As^{V}$$

yellow colorless

This reaction has since found numerous applications, being an especially favorable indicator reaction: it can be readily monitored by photometry, potentiometry (change in Ce^{IV}: Ce^{III} ratio), biamperometry, and thermometry.

The iodine-azide reaction mentioned in Section 1 which is catalyzed by divalent sulfur has also been frequently utilized.

Some metals such as copper and manganese catalyze the decomposition of hydrogen peroxide; this reaction can be followed particularly well by thermometry.

The reviews cited[4-6] list numerous examples of such reactions, and a selection of recent developments is presented in Table 1.

Table 1. Some examples of redox reactions.

Substance	Reaction	Ref.
Vanadium in blood	*p*-Hydrazinobenzenesulfonic acid + ClO_3^-	[12]
Chromium	*o*-Dianisidine + H_2O_2	[13]
Molybdenum in plants	$I^- + H_2O_2$	[14]
Manganese	Alizarin S + H_2O_2	[8]
Iron in plants	*p*-Phenetidine + H_2O_2	[15]
Ruthenium in minerals	*o*-Dianisidine + IO_4^-	[16]
Osmium, ruthenium	α-Naphthylamine + NO_3^-	[17]
Osmium	$As^{III} + BrO_3^-$	[18]
Cobalt in reactor cooling water	Alizarin red S + H_2O_2	[19]
Copper	$S_2O_3^{2-} + Fe^{III}$	[20]

An interesting group of redox reactions warranting mention are the peroxide oxidation of luminol or lucigenin catalyzed by various metals (copper, manganese, chromium, cobalt) during which chemiluminescence occurs. The light emitted can easily be measured by photometry (possibly with the aid of a photomultiplier). In this way 26 pg/ml of chromium(III) are determinable by a flow technique[21] (1 picogram = 10^{-12} g).

2.2. Ligand Exchange Reactions

A fitting example is the silver ion-catalyzed exchange reaction between hexacyanoferrate(II) und 2,2'-bipyridine (bipy)[22]:

$$[Fe(CN)_6]^{4-} + 3\,bipy \xrightarrow{Ag^+} [Fe(bipy)_3]^{2+} + 6CN^-$$

In similar manner, traces of mercury in the air have been determined by hexacyanoferrate and nitrosonaphthol[23].

An exchange reaction involving complexes with multidentate ligands is the following process which has been called a "coordination chain reaction": copper-edta and and nickel-trien react together *via* ligand exchange to form copper-triene and nickel-edta; the reaction rate is greatly accelerated by small amounts of additional complexing agent ethylenediaminetetraacetic acid (edta) or *N,N'*-bis(2-aminoethyl)ethylenediamine ("triethylenetetramine", trien). The course of reaction can be conveniently followed by photometry[24].

2.3. Enzyme Reactions

The determination of enzyme activity is based on the same principles as that of the catalytic activity of inorganic substances. Enzyme reactions are employed primarily in clinical and biochemical laboratories.

Apart from enzyme activity, substrates, *i.e.* reactants, can also be determined highly selectively *e.g.* glucose by means of glucose oxidase:

$$Glucose + H_2O + O_2 \xrightarrow{\text{glucose oxidase}} Gluconic\ acid + H_2O_2$$

$$H_2O_2 + 2I^- + 2H^+ \xrightarrow{Mo} I_2 + 2H_2O$$

This represents an example of the coupling of two catalyzed reactions. The rate of iodine formation provides a measure of the glucose concentration[25].

As in the analysis of other catalysts, any substance having a positive or negative effect on the catalytic (here enzymatic) activity, can be determined. Various metal ions inhibit enzymes; for instance, pg quantities of silver or mercury can be determined by inhibition of alcohol dehydrogenase[26]. Moreover, non-metals can also be determined by this method: pig liver esterase is significantly inhibited by traces of fluoride[27]. Particular significance may be attributed to the quantitative determination of pesticides (*e.g.* Lindane, Aldrin, DDT) by way of their inhibitor action on enzymes such as lipase, phosphatase, and above all cholinesterase[28].

Reactivation of inhibited enzymes can be utilized for quantitative determination of the reactivator; thus traces of cyanide and sulfide are determined by measuring the reactivation of invertase inhibited by mercury[29].

On removal of the metal ion from a metalloenzyme (*e.g.* zinc from alkaline phosphatase by ethylenediaminetetraacetic acid) there is a loss of enzyme activity; slight traces of the same metal (in this case zinc) reactivate the enzyme. This provides a highly sensitive determination of the activator[30].

The extensive field of enzymatic analysis is considered at great length in the books by *Bergmeyer*[31] and *Guibault*[28]; just a few indications of possible application will suffice in this article.

3. Determinations Employing Closed and Open Systems

A whole series of possible methods are available for the quantitative interpretation of the catalyzed reaction for determining the catalyst. An initial distinction is made between "closed" and "open" systems: closed systems are those in which there is no external intervention during the reaction; neither reactant nor product are added or removed once the catalytic reaction has started.

In open systems, on the other hand, reactants are added and/or products removed during the reaction.

3.1. Closed Systems

The general procedure described in Section 1 illustrates the use of a closed system. Let us now briefly consider three further methods of this kind.

The visual procedure referred to as the "simultaneous comparison method" by *Bognar* (1963)[32] is based on a simple experimental set-up described as early as 1922 by *Hahn* and *Leimbach:* equal volumes of a solution of reactant A and increasing known amounts of catalyst K are pipeted into a series of test tubes; the sample solution having an unknown concentration of K is then placed in one of these test tubes. Immediately, equal volumes of a solution of reactant B are added simultaneously, thus starting the reaction in all cases.

Observation of changes occurring in the individual mixtures—*e.g.* coloration, decoloration—reveals which of the standards corresponds most closely to the sample in its behavior. Under identical conditions, equal changes clearly also mean corresponding catalyst concentrations. This method utilizes a "dynamic colorimetric standard scale".

Since all reactions proceed simultaneously under the same conditions there is no need for thermostating; moreover, neither time nor concentration have to be measured directly.

While this "simultaneous comparison method" probably represents the nearest approach to the "tangent method", systems of the "Landolt type" provide an opportunity of carrying out processes which can be regarded as "fixed concentration methods".

A slow reaction is connected with a fast one by the product X of the former (slow) reaction. Hence it follows that X can only be present in the free state once all the R has been consumed, *i.e.* the system must be deficient in R.

$$\begin{aligned} A + B &\rightarrow X + Y \quad \text{slow} \\ X + R &\rightarrow E \quad\quad \text{fast} \end{aligned}$$

If the first reaction can be accelerated by a catalyst, then the time elapsing between the start of reaction and the appearance of free X, the "induction period", is a measure of the catalyst concentration: the shorter the induction period the greater is the catalyst concentration.

This "chronometric" method has been successfully applied to the determination of a series of catalytically active metal ions (Fe, Mo, Zr, V)[33]. For example:

$$BrO_3^- + 5Br^- + 6H^+ \xrightarrow[pH \approx 5]{V} 3Br_2 + 3H_2O$$

$$3Br_2 + 3\,\text{ascorbic acid} \rightarrow 6Br^- + 6H^+ + 3\,\text{dehydroascorbic acid}$$

This is a self-regenerating system, the reactant B (Br^-) of the first reaction being re-formed in the second reaction. Only after all the ascorbic acid has been consumed does bromine appear momentarily and can be detected, for example, with a fluorescence indicator (trypan red)[34].

The next procedure we shall consider is a catalytic difference method: two vessels contain equal amounts of a reaction mixture A + B and the catalyst serving to accelerate the inhibited reaction, albeit at different concentrations (sample K_p and standard K_v); thus the two systems differ only in the concentration of catalyst

$$\text{sample:} \quad A + B \xrightarrow{K_p} X + Y$$

$$\text{standard:} \quad A + B \xrightarrow{K_v} X + Y$$

Whatever property of the system is employed for monitoring the reaction course—*e.g.* the extinction or the potential—the difference between the two measured values will always initially be zero. Subsequently, however, the differing catalyst concentrations in the two mixtures will lead to a steadily increasing difference which rises to a maximum; finally, after reaction has reached completion in the two systems (this may take a considerable time) the difference is again zero.

This change in the difference with time will provide some information about the ratio of the catalyst concentrations, either from the height of the maximum, from the area under the curve, or from the slope of the curve leading up to the maximum; hence it should be possible to establish the unknown concentration in the sample.

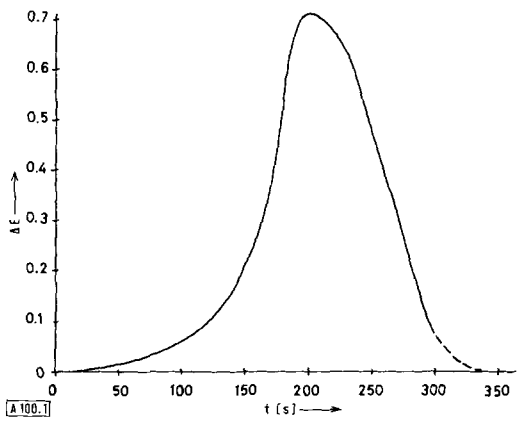

Fig. 1. Variation of extinction difference with time.

Figure 1 shows a curve obtained in such an experiment, namely the photometrically recorded difference in extinction in the copper-catalyzed reaction

$$2Fe^{III} + 2S_2O_3^{2-} \xrightarrow{Cu} 2Fe^{II} + S_4O_6^{2-}$$

The intensely red complex of iron(III) with thiocyanate serves as indicator of the course of reaction.

This reaction was utilized for the determination of copper (1—25 μg in 10 ml; standard always 5 μg). It proved most convenient to employ the maximum difference in extinction, occurring within minutes, in evaluation of the results; once this value has been recorded measurement can stop, there being no need to record the entire curve. The desired copper concentration can be extrapolated from a calibration curve. Measurement can readily be performed in a Lange colorimeter[20, 35].

In such difference determinations the reaction course can also be followed by potentiometric[20], thermometric, and conductometric methods[36].

3.2. Open Systems

Flow, "steady state", and "stat" methods should be mentioned under this heading. They all have in common that the course of reaction is subjected to external influence by addition of reactants and/or removal of products.

In the "stat" methods[37] a given state of the system is arbitrarily imposed and maintained during the reaction by addition of a reagent. The system itself controls this addition; the rate of addition of reagent necessary for maintaining the given state provides a measure of the reaction rate and hence for the catalyst concentration to be determined. The factor maintained, and thus serving the control function, is a physical property of the system dependent upon the concentration of a reactant, a product, or the ratio of reactant to product.

Let us again consider the general reaction

$$A + B \xrightarrow{K} X + Y$$

and assume B to be present in considerable excess so that its concentration can be regarded as constant; then, if the reaction course is followed by measurement of A:

$$-\frac{dC_A}{dt} = kC_K C_A$$

Now if A is supplied at the same rate at which it is consumed in the reaction, it follows, because C_A is no longer a variable, that:

$$-\frac{dC_A}{dt} = k'C_K$$

This is therefore a reaction of "quasi"-zero order: the reaction rate remains constant over a relatively long period, *i.e.* beyond the initial state, and the rate of addition is proportional to the catalyst concentration C_K.

An example utilizing photometric control may serve as an illustration[38]: manganese catalyzes the oxidation of malachite green by periodate (at pH = 3–4), reaction being accompanied by decoloration:

$$IO_4^- + \text{malachite green} \xrightarrow{Mn} \text{colorless product}$$

A schematic diagram of the apparatus, termed "extinctiostat" ("absorptiostat") is shown in Figure 2: the thermostated

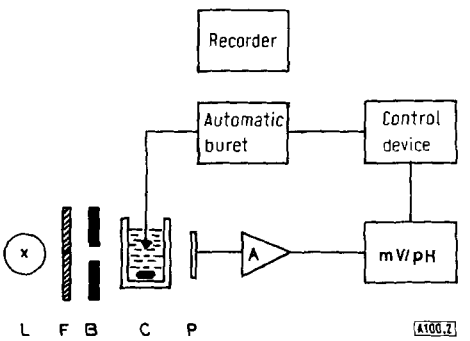

Fig. 2. Extinctiostat (absorptiostat). L, light source; F, monochromatic filter; B, iris diaphragm; C, thermostated cell; P, photocell; A, amplifier.

cell C contains the reaction mixture (malachite green + IO_4^-) with the Mn solution to be determined; L is the light source (here 619 nm). The signal from the photocell (P) is amplified (A), registered as a potential by a mV meter and fed to the control device. Here the measured value is compared with a given set potential. This set potential corresponds to a certain set extinction in the cell and thus logically to a definite selected concentration of malachite green. The difference between the set and the actual potential, and thus between the set and actual concentration of malachite green, arising in the course of the reaction, is corrected by a command to the buret: the deficit at any time is compensated by addition

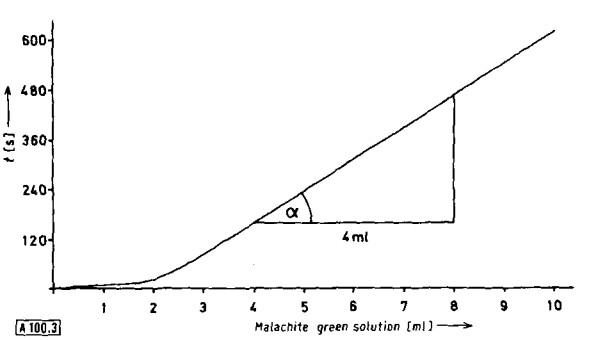

Fig. 3. Curve plotted for 7.5 μgMn/45 ml catalyzing the oxidation of malachite green by periodate.

of a corresponding amount of malachite green standard solution. The recorder registers the rate of addition (ml/min) of standard solution; this provides a measure of the catalyst concentration (Mn) to be determined. A curve of this kind as registered by the recorder is shown in Figure 3. Evaluation is based on the cotangent of α (vol/time) taken from the plot. A calibration graph is plotted with several cotangent α values for known manganese concentrations.

The pH stat procedure[39] and methods employing a potentiostat[40], a biamperostat[41], and a luminostat[42] all function in analogous manner; in the last-named case the chemiluminescence occurring on reaction of luminol with hydrogen peroxide is maintained constant by controlled addition of H_2O_2. Metals catalyzing this reaction, *e.g.* copper, can be determined by this technique.

While all these "stat" methods involve addition of some reagent controlled by a change of a physical phenomenon in the system itself, "steady-state" methods entail admixture of a reactant at a constant rate. This technique was employed in a similar form by *Pearson* and *Piette*[43] for determining kinetic data of noncatalyzed reactions. To a system containing one of the two reactants (A) in great excess as well as the catalyst (K) to be determined is added the other reactant (B) at constant rate by means of a motor-driven piston buret. The reaction A+B starts directly upon addition of the first small portion of B, albeit very slowly owing to the initially very low concentration of reactant B in the system. This means, however, that not even the minute amount of B will be completely consumed.

Since B is added continuously, its concentration and hence also the rate of reaction A+B will increase; and so will the consumption of B.

After some time a stage is reached at which precisely the same amount of B is consumed per unit time as is added from the buret. A steady state of the system—with regard to the concentration of B—is then attained and will persist for some time.

Whatever physical property, whatever phenomenon is chosen for measuring the steady-state concentration of B, *e.g.* the extinction or the potential, it serves as a measure for the reaction rate and thus, under otherwise identical conditions, as a measure for the concentration of catalyst to be determined. As always, a calibration graph is used in evaluation; the reciprocal value of the steady state concentration (or the corresponding measurement, *e.g.* extinction or potential) is plotted *versus* the catalyst concentration.

In this way it was possible, for example, to determine between 60 and 650 ng of iodide using the Sandell-Kolthoff reaction between arsenic(III) and cerium(IV): the iodide sample is added to an excess of arsenic(III) and an approximately 10^{-2} M solution of cerium(IV) added from a motor-driven piston buret at a rate of about 10 µl/min to a reaction volume of about 10 ml. The change in optical density (at 420 nm) is recorded. After a few minutes a steady state is attained, the extinction remaining unaltered[44].

In the methods just described one of the reactants is added to the other, the rate of addition being either constant or regulated by the system itself.

It is, of course, also possible not only to add a reagent but to simultaneously remove an equal volume of reaction solution. This is practiced in flow methods. A flow apparatus is schematically depicted in Figure 4.

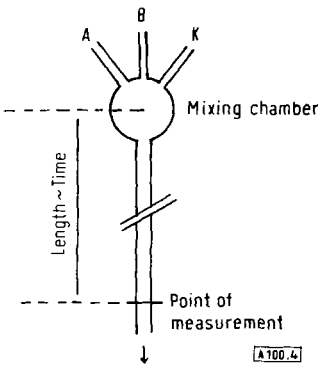

Fig. 4. Schematic representation of flow tube. A, B, reactants; K, catalyst.

The reactants A and B and the solution of the catalyst K to be determined flow separately into a mixing chamber, whence they enter a flow tube. At a given point, some property of the system (potential, optical density, *etc.*) is continuously monitored. The distance between the mixing chamber and the point of measurement corresponds to a certain fixed time, provided of course that the flow rate is constant.

The value measured provides a measure of the catalyst concentration.

The flow technique is well suited to continuous analysis, any change in catalyst concentration will clearly alter the value measured.

Although this kind of kinetic method has been known for over five decades there are only few analytical applications. *Wilson*[45] used such an experimental set-up for continuous determination of molybdenum (1—50 µg) with the aid of the reaction of peroxoborate with iodide.

Whereas steady-state, but different, concentrations of reactants and products will be established at different positions of the flow tube if the reaction conditions remain unchanged, that variant of the flow technique employing thorough back mixing ("capacity flow cell")[46] is characterized by attainment of an effectively uniform steady-state concentration of the reactants and products throughout the entire reaction vessel. This method will now be illustrated by the manganese-catalyzed oxidation—and hence decoloration—of alizarin S by hydrogen peroxide[8]: the manganese to be determined and

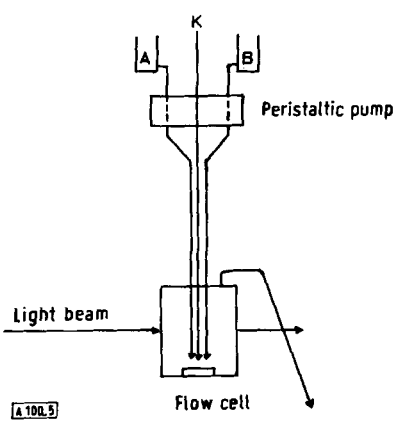

Fig. 5. Schematic representation of a flow cell. A, B, K, see Fig. 4.

the reactants alizarin S and hydrogen peroxide flow separately into a flow cell (cf. Fig. 5) where they are immediately thoroughly mixed. After some time a steady state is established

with regard to the concentration of all reactants and products. The concentration of alizarin S is continuously monitored by photometry and recorded. It affords a measure of the amount of catalyst: the higher the concentration of manganese the lower the concentration of alizarin S.

As with all other catalytic-kinetic methods, these flow methods can also be used for determining inhibitors, activators, reactivators.

Special flow techniques have also been developed for following very fast reactions (*e.g.* stopped flow, accelerated flow methods)[2]; however, they have only rarely been employed for analytical purposes.

The flow technique is also well suited to automation. A detailed report has recently been published on automation and instrumentation of kinetic analytical procedures employing open and closed systems[47].

4. Catalytic End Point Indication in Volumetric Analysis

All the methods discussed so far require quantitative determination of catalytic activity in order to determine the catalyst itself or, indirectly, an inhibitor, activator, or reactivator. On use of catalyzed reactions for end point determination in volumetric analysis, it suffices to establish qualitatively that the catalyst is present at a concentration high enough to detectably enhance the rate of an indicator reaction. During the past few years catalytic reactions have been employed for indication purposes in volumetric determinations[3]. A review of this comparatively young field has recently been written by *Hadjiioannou*[48].

The volumetric solution (K) which catalyzes the reaction between substances A and B is added from a buret. This volumetric solution can be used for titration *versus* a substance (an inhibitor) which drastically impairs the activity of the catalyst K, possibly by precipitation or complexation. The first excess drop of solution from the buret (*i.e.* of catalyst K) accelerates the indicator reaction between A and B; this is exploited for end-point detection.

The method is illustrated by the precipitation titration of silver with potassium iodide standard solution: to the silver solution to be determined is added yellow cerium(IV) sulfate solution and arsenic(III); titration with 0.1 N potassium iodide is then performed with vigorous stirring(!). Iodide ion is precipitated as silver iodide. The first excess potassium iodide catalyzes the cerium-arsenic indicator reaction and the yellow cerium(IV) solution is immediately decolorized[49].

Chloride, bromide, iodide, and thiocyanate can also be determined in this way by back titration.

Such catalytic end-point determinations have the advantage that the excess of titration reagent is not consumed in a stoichiometric reaction with an indicator but merely acts as a catalyst; a very small excess of volumetric reagent is able to catalyze reactions of comparatively large amounts of the reagent mixture serving as indicator.

An example of reducing catalytic activity (inhibition) as a result of complex formation is provided by the titration of ethylenediaminetetraacetic acid with a cobalt volumetric solution; oxidation of Tiron by peroxoborate (gold coloration) serves as indicator reaction[49].

The end point does not have to be determined visually; any physical method permitting determination of changes accompanying the occurrence of the indicator reaction in the system can be utilized. Thus catalytic end-point determinations employing potentiometry[50], biamperometry, photometry[51], and thermometry[52, 53] have all been described.

The last-mentioned procedure appears especially interesting since it is not the slight evolution of heat during the actual titration reaction (catalyst + inhibitor) which serves for end-point recognition, but instead the much greater one accompanying the indicator reaction (A + B) which occurs once the end-point is passed.

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

trans-Pentacarbonylrhenio(phenylcarbyne)tetracarbonylmolybdenum: A Transition Metal Carbyne Complex Containing a Metal-Metal Bond[1]

By *Ernst Otto Fischer*, *Gottfried Huttner*, *Tassilo Lothar Lindner*, *Albin Frank*, and *Fritz Roland Kreissl*[*]

trans-Bromo(tetracarbonyl)carbyne complexes of chromium, molybdenum, and tungsten[2] react with sodium pentacarbonylmanganate(−I)[3a] and -rhenate(−I)[3b] *via* halogen/carbonylmetal exchange at low temperature to give new dinuclear carbyne compounds:

$$(CO)_5M'Na + BrM(CO)_4{\equiv}CC_6H_5 \xrightarrow[-25\,^\circ C]{THF} (CO)_5M'\text{–}M(CO)_4{\equiv}CC_6H_5 + NaBr$$

M' = Mn, Re; M = Cr, Mo, W

The yellow to orange colored products are readily soluble in both polar and apolar organic solvents and exhibit greater thermal stability than the corresponding bromo complexes. Their stability increases on going from the Mn—Cr to the Re—W derivatives. All the compounds were verified by total elemental analysis, by IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectrometric investigations, and by X-ray structure analysis. We selected $(CO)_5Re—Mo(CO)_4{\equiv}CC_6H_5$ as representative for characterization of the new type of compound.

In the region of the ν_{CO} frequencies the IR spectrum (in *n*-hexane) of this complex displays the five bands expected (2 E and 3 A_1)[4] for the carbyne ligand in an axial position at 2104 m, 2049 m, 2019 vs, 1975 s, and 1968 s cm^{-1}. The ^{1}H-NMR spectrum contains the multiplet due to the phenyl protons at 7.63 ppm (in CD_2Cl_2, −20 °C, TMS internal standard). The ^{13}C-NMR findings accord with our ideas about the structure of the dinuclear carbyne complex: Owing to Br/$(CO)_5$Re exchange the signals of the carbyne carbon atom, and also of the carbon atom belonging to the CO group attached to molybdenum, are shifted downfield relative to the starting complex[5]; the carbonyl signal of the $(CO)_5$Re group appears as a very broad signal as a result of the nuclear spin of 5/2 in the case of both rhenium isotopes; the four signals of the aromatic carbon atoms are observed in the usual range [in [D_8]-THF, relative to solvent (67.32 ppm), δ = 293.98 ($C_{carb.}$), 215.44 (CO_{Mo}), 199.40 br (CO_{Re}), 146.23, 133.13, 132.16, 129.35 ppm (C_6H_5)].

The structure of the new compound was confirmed by X-ray structure analysis [973 independent reflections ("Syntex P21"); solution with "Syntex XTL" (R_1 = 0.051)]: space group C2/c; a = 1084.4, b = 1712.7, c = 1042.4 pm; β = 91.2°; Z = 4.

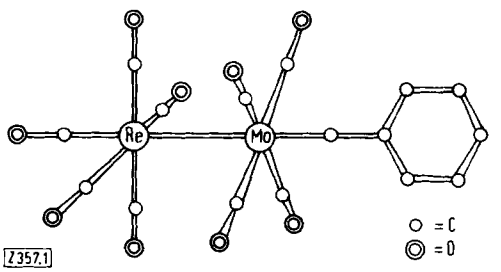

Fig. 1. Structure of $(CO)_5Re—Mo(CO)_4{\equiv}CC_6H_5$.

On account of the space group symmetry (twofold axis of rotation) the *trans*-CO—Re—Mo—$C_{carbyne}$ grouping is strictly linear. The Re—Mo bond having a length of 311.1 ± 0.2 pm is to be regarded as a single bond (for comparison: η-$C_5H_5(CO)_3Mo—Re(CO)_5$ 312 pm[6]). The Mo—$C_{carbyne}$ distance is 183.5 ± 2.5 pm and thus corresponds, within the limits of error, to the sum of the triple bond radii of Mo≡Mo[7] and C≡C[8] (122.4 + 60.5 = 182.9 pm). As in the decacarbonyl compounds of Mn[9a] and Tc[9b], the equatorial carbonyl groups are in a staggered arrangement and bent toward each other (by 9.6°).

Procedure:

All operations should be carried out under nitrogen with dried (Na, P_4O_{10}) and N_2-saturated solvents. A THF solution of $NaRe(CO)_5$ (1.75 g, 5 mmol) is reacted at −25 °C with $BrMo(CO)_4CC_6H_5$ (1.89 g, 5 mmol) in THF (25 ml). The mixture is stirred for 30 min and the solvent then removed in a high vacuum. The crude product obtained by extraction with pentane is purified by chromatography in pentane/methylene chloride on silica gel at −20 °C. Recrystallization from pentane affords analytically pure $(CO)_5Re—Mo(CO)_4{\equiv}CC_6H_5$, orange crystals, m.p. 85—87 °C; yield 32%.

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$NaRe(CO)_5$, 33634-75-2; *trans*-$BrMo(CO)_4CC_6H_5$, 50726-29-9; $(CO)_5Re—Mo(CO)_4{\equiv}CC_6H_5$, 58312-75-7

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Bromyl Cation, $[BrO_2]^+$ [**]

By *Eberhard Jacob*[*]

Dedicated to Professor Josef Goubeau on the occasion of his 75th birthday

The co-condensation of highly reactive components at low temperatures[1] offers a means of moderating otherwise uncontrollable reactions and of directing them along preparatively interesting pathways. This approach has now permitted the first generation and stabilization of the bromyl cation as the fluoroantimonate *(2a)* by slow warming of a co-condensate of bromyl fluoride *(1)*[2] and an excess of antimony pentafluoride, prepared at −196 °C, to room temperature in a high vacuum.

$$\underset{(1)}{BrO_2F} + SbF_5 \xrightarrow{SbF_5} \underset{(2a)}{[BrO_2]^+[SbF_6(SbF_5)_{1.24}]^-}$$

An inhomogeneous distribution[3] of *(1)* in the co-condensate is manifested in a red coloration owing to formation of the thermally more stable dibromine salt *(3)*:

$$9\underset{(1)}{BrO_2F} + 5\,SbF_5 \rightarrow 4\underset{(3)}{[Br_2]^+[SbF_6]^-} + \underset{(4)}{[BrF_4]^+[SbF_6]^-} + 9O_2$$

$[BrO_2]^+$ is already formed at temperatures below −80 °C in a solid state reaction. Compound *(2a)* is difficult to obtain colorless (usually yellowish because of traces of dark red *(3)*). It is stable at room temperature (dissociation pressure $<10^{-3}$ torr). Atmospheric moisture or warming to 80 °C effects rapid decomposition. Thermal degradation leads by way of evolution of oxygen to *(3)* and *(4)* as primary products. Vacuum pyrolysis of *(2a)* in the presence of an excess of sodium fluoride permits precise determination of the amount of $[BrO_2]^+$ in *(2a)*.

$$3(2a) + 6.72\,NaF \xrightarrow{250\,^\circ C} 6.72\,NaSbF_6 + 3O_2 + BrF_3 + Br_2$$

The salt-like character of *(2a)* is apparent from its IR and Raman spectra. In addition to the characteristic frequencies expected for $[Sb_2F_{11}]^-$ and $[Sb_3F_{16}]^-$[4], the only other bands found showed the frequency shifts calculated for a bent $[BrO_2]^+$ species having C_{2v} symmetry on isotope substitution[5]. The fundamental vibrations of the cation reveal the similarities expected for isoelectronic species with those of monomeric selenium dioxide (cf. Table 1).

Table 1. Fundamental vibrations of the bromyl cation and of selenium dioxide [a].

	$\nu_1(A_1)$		$\nu_2(A_1)$		$\nu_3(B_1)$	
	IR	Raman	IR	Raman	IR	Raman
$[Br^{18}O_2]^+$	832 vw	825 s	354 s	355 m	897 s	889 m
$[BrO_2]^+$	876 vw	865 s	375 s	375 m	930 s	932 m
SeO_2 [6]	922 w	933 s	373 s	382 m	965 s	967 m

[a] Monomeric SeO_2 in an argon matrix.

Bromyl hexafluoroarsenate, $[BrO_2]^+[AsF_6]^-$ *(2b)*, arises on co-condensation of *(1)* and arsenic pentafluoride at −196 °C and warming to −50 °C. In a high vacuum *(2b)* volatilizes above −35 °C with decomposition. The IR spectrum of a thin film of this salt shows the fundamental vibrations of the cation and the anion[7].

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[**] Low-temperature co-condensation of fluorine compounds, Part 1.

Procedure:

BrO_2F (3.1 g, 24 mmol) from a storage vessel cooled to −7 °C and SbF_5 (28.3 g, 130 mmol) are simultaneously passed through two concentric tubes into the lower part of a 2-l stainless steel vessel cooled with liquid nitrogen, where they condense. Throughout the co-condensation (1 h), warming (3 h), and pumping off of excess SbF_5 at room temperature to constant weight a maximum vacuum is maintained. The reaction product is collected with exclusion of moisture; yield 8.6 g (13 mmol) $[BrO_2]^+[SbF_6(SbF_5)_{1.24}]^-$.

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CAS Registry numbers:
(1), 22585-64-4; *(2a)*, 58409-46-4; *(2b)*, 58409-47-5;
SbF_5, 7783-70-2; $[Br^{18}O_2]^+$, 58384-59-1

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Xenon Oxide Difluoride, $XeOF_2$ [**]

By *Eberhard Jacob* and *Robert Opferkuch*[*]

Dedicated to Professor Josef Goubeau on the occasion of his 75th birthday

We have been able to synthesize and isolate a xenon oxide difluoride which has formerly only been detected by spectroscopy[2]; the method employed was low-temperature co-condensation. A solid co-condensate of xenon tetrafluoride and water (molar ratio 1 : 1.1) transforms into xenon oxide difluoride between −80 and −50 °C.

$$XeF_4 + H_2O \longrightarrow XeOF_2 + 2\,HF$$

In order to avoid the reaction[3]

$$XeF_4 + 2H_2O \rightarrow Xe + O_2 + 4HF$$

the hydrogen fluoride liberated on hydrolysis is continuously pumped off.

$XeOF_2$ is a pale yellow nonvolatile solid which is stable up to −25 °C. It decomposes on slow warming (≈20 °C/h) to −15 °C with decoloration according to [4]:

$$2XeOF_2 \rightarrow XeO_2F_2 + XeF_2$$

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[**] Low-temperature co-condensation of fluorine compounds, Part 2.–Part 1: ref. [1].

This thermolysis of $XeOF_2$ in vacuum can be utilized for synthesis of the difficultly accessible XeO_2F_2, since the other product formed, XeF_2, sublimes at $-15\,^{\circ}C$. At $25\,^{\circ}C$, XeO_2F_2 slowly decomposes to XeF_2 and O_2.—Faster warming of $XeOF_2$ ($>20\,^{\circ}C$/h) leads to an explosion. Condensation of SbF_5 or AsF_5 onto $XeOF_2$ initiates explosive decomposition even at $-196\,^{\circ}C$. This also happens in contact with solid mercury. For indirect analysis of $XeOF_2$ the products of controlled thermolysis were therefore reacted with quartz wool:

$$XeO_2F_2 + XeF_2 + SiO_2 \rightarrow 2Xe + 2O_2 + SiF_4$$

The fluorine content (calc. 20.5 %, exp. 20.6 %) was obtained from the consumption of SiO_2 and from the fluoride analysis after hydrolysis of the SiF_4, the results of the two procedures showing mutual agreement.

The IR spectra of $XeOF_2$ and $Xe^{18}OF_2$ (99 %) were recorded for thin films ($-30\,^{\circ}C$)[5]: 751 (705) m, 715 (668) vw, 510 (515) vs, 498, 490 (496, 488) s, 210 s. The Raman spectra (powder spectra at $-196\,^{\circ}C$) show the following lines[5]: 751 (714), 1.2—1.9; 738 (700), 10; 497.5 (497.5), 6.2—6.5; 469.5 (469.5), 6.3—6.4; 299.5 (291), 0.8—0.9; 288 (278.5), 0.6; 171.5 (161.5), 1.5—1.6; 154 (—), 0.9; 135 (137), 1.0; 111.5 (104), 2.2. The frequency 715—750 cm^{-1}, which is very low for a Xe—O stretching vibration, contraindicates the presence of monomeric $XeOF_2$ having C_{2v} symmetry[2], instead suggesting oxygen bridging.

Procedure:

XeF_4 (1.53 g, 7.4 mmol) and H_2O (144 mg, 8 mmol) are simultaneously passed from cooled storage vessels (0 and $-22\,^{\circ}C$, respectively) *via* two concentric tubes into a vessel (100 ml, Teflon PFA$^+$) cooled to $-196\,^{\circ}C$ under dynamic vacuum conditions. Raising of the temperature to $-80\,^{\circ}C$ initiates the reaction (yellow coloration!). The reaction proceeds faster at $-63\,^{\circ}C$ (2 h) and goes to completion at $-47\,^{\circ}C$ (1 h) (liberation of HF ceases). The product $XeOF_2$ (1.3 g, 7 mmol) can be manipulated safely below $-40\,^{\circ}C$ in a dry atmosphere (glovebox).

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CAS Registry numbers:
$XeOF_2$, 13780-64-8; $Xe^{18}OF_2$, 58384-58-0; XeO_2F_2, 13875-06-4; XeF_4, 13709-61-0

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[3] Hydrolysis of XeF_4 in anhydrous HF at $-80\,^{\circ}C$ (molar ratio 1:1) proceeds exclusively *via* liberation of Xe and O_2 since the solubility conditions cause a permanent excess of water.
[4] The decomposition products were identified by IR spectroscopy.
[5] Data in cm^{-1}, values for $Xe^{18}OF_2$ given in parentheses.

Hexafluororhenium(VII), $[ReF_6]^+$

By *Eberhard Jacob* and *Manfred Fähnle*[*]

Dedicated to Professor Josef Goubeau on the occasion of his 75th birthday

In contrast to our previous knowledge[1], rhenium hexafluoride and rhenium heptafluoride exhibit distinct differences in their reactions. ReF_7, but not ReF_6, reacts with photochemically generated fluorine atoms in an argon or fluorine matrix at 27 K[2] according to

$$ReF_7 + F \rightarrow ReF_6 + F_2$$

Hence it follows that the first bond dissociation energy of ReF_7 is lower than the dissociation energy of the fluorine molecule, while that of ReF_6 is larger. Whereas fluorine atoms are unable to oxidize ReF_6, the very pronounced electron affinity of platinum hexafluoride should permit formation of the hexafluororhenium(VII) cation. Decoloration of the dark red vapor of PtF_6 by ReF_6 in a nonstoichiometric reaction with formation of a red solid as sole product can only be rationalized by assuming the production of $[ReF_6]^+[PtF_6]^-$. On the other hand, it is not surprising that no reaction takes place between ReF_7 and PtF_6 in the absence of light.

ReF_7 should therefore be capable of functioning as a fluoride donor. Thus, unlike ReF_6, it reacts with antimony pentafluoride to form hexafluororhenium(VII) fluoroantimonates.

$$\underset{(1)}{[ReF_6]^+[SbF_6]^-} \longleftarrow ReF_7 + SbF_5 \xrightarrow{SbF_5} \underset{(2)}{[ReF_6]^+[Sb_2F_{11}]^-}$$

The hexafluoroantimonate *(1)* is formed on one day's heating of an excess of ReF_7 with SbF_5 at $250\,^{\circ}C$ in a fluorine atmosphere. During the reaction and cooling the temperature of the nickel reactor must be uniform. The undecafluorodiantimonate *(2)* is most conveniently prepared by high-pressure fluorination of a stoichiometric rhenium/antimony mixture at $400\,^{\circ}C$ and subsequent homogenization (annealing at $200\,^{\circ}C$). The compositions of the cream-colored compounds *(1)* and *(2)* were established by quantitative synthesis. *(1)* does not have a measurable vapor pressure at $25\,^{\circ}C$. Vacuum thermolysis of *(2)* at $90\,^{\circ}C$ affords a product containing less antimony, but does not lead to *(1)*. Hydrolysis of *(1)* in air is surprisingly slow, that of *(2)* much faster. The hydrolysis products are colorless solutions containing perrhenate. The pronounced stability of *(1)* can be attributed to very favorable lattice energies (only octahedral ions).

Apart from the bands characteristic for $[SbF_6]^-$[3] and $[Sb_2F_{11}]^-$[4], the vibrational spectra of *(1)* and *(2)* display five bands which are assigned to the octahedral species $[ReF_6]^+$[5]; three Raman lines at 797 (10), 734 (4.6—4.9), and 359 (2) cm^{-1} correspond to fundamentals $\nu_1(A_{1g})$, $\nu_2(E_g)$, and $\nu_5(F_{2g})$; two IR bands at 783 (s) and 353 (m) cm^{-1} belong to the representation F_{1u} (ν_3 and ν_4). The fundamental modes of $[ReF_6]^+$ thus appear at considerably higher wave numbers than those of all metal hexafluorides. Having a value of 6 mdyn/Å[6] the valence force constant is significantly larger than those of WF_6 and ReF_6 (*ca.* 5.1 mdyn/Å); it is indicative of a multiple bonding component of the Re—F bond arising from the deficiency of electrons at the central atom[7].

$[ReF_6]^+$ is the first fluorocation of a transition metal. The fluorides of the main group elements have fluoride donor properties when the difference in electronegativity between the central atom and fluorine is low[8]. Thus the donor action of ReF_7 indicates a high electronegativity of Re^{VII}.

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CAS Registry numbers:
(1), 58409-50-0; *(2)*, 58409-51-1; ReF_7, 17029-21-9; SbF_5, 7783-70-2

[1] *J. H. Canterford, T. A. O'Donell*, and *A. B. Waugh*, Aust. J. Chem. *24*, 243 (1971).
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[5] The cation bands show uniform weakening on partial hydrolysis of *(1)* and *(2)*.
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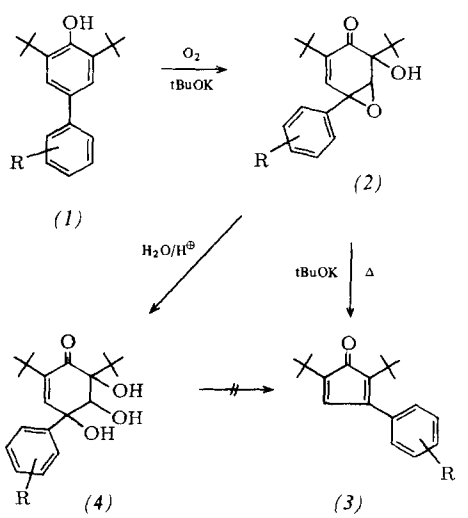
Synthesis of 3-Aryl-2,5-di-*tert*-butyl-2,4-cyclopentadienones by Base-Catalyzed Oxygenation of 4-Aryl-2,6-di-*tert*-butylphenols

By *Akira Nishinaga, Toshio Itahara, Teruo Matsuura, Anton Rieker*, and *Dieter Koch*[*]

Sterically hindered phenols are employed as antioxidants. Hence, the investigation of their autoxidation and oxidative degradation is of interest.

The potassium *tert*-butoxide (tBuOK) catalyzed oxygenation of *tert*-butylated phenols depends strongly on the solvent: in hexamethylphosphoric triamide (HMPA) or dimethylformamide (DMF) molecular oxygen attacks only the *p*-position and in *tert*-butanol (tBuOH) only in the *o*-position, giving in each case exclusively epoxy-*p*-quinols and epoxy-*o*-quinols, respectively[1,2].

We now find that 4-aryl-2,6-di-*tert*-butylphenols *(1)* are not oxygenated in the presence of tBuOK in DMF, HMPA or methanol, but are very readily in tBuOH at 75°C. The latter reaction affords a novel and convenient route to the 3-aryl-2,5-di-*tert*-butyl-2,4-cyclopentadienones *(3)*. The structure of compounds *(3)* is confirmed by analytical and spectroscopic data (Table 1).



Other products isolated in the reaction are the epoxy-*o* quinols *(2)*. Their structures are given by analytical and spectroscopic data and by comparison with analogous compounds[2]. If higher yields of the epoxy-*o*-quinols *(2)* are desired the reaction is better carried out at 0°C.

When *(2a)* is heated in tBuOH containing tBuOK under N_2 *(3a)* is formed in almost quantitative yield, whereas *(4a)* does not react under these conditions. The compound *(2b)* behaves analogously. These results show that *(3)* is formed *via (2)* in the base-catalyzed oxygenation of *(1)*.

Electron-donating substituents accelerate the reaction, electron withdrawing and sterically hindered substituents retard it. The opening of the epoxy ring in *(2)* appears to be affected likewise by the substituents in the aryl ring. This is supported by the fact that the yields of *(3)* increase at the cost of the epoxy-*o*-quinols *(2)* when the duration of oxygenation is prolonged. The reaction path *(2)*→*(3)* promoted by bases is characteristic for aromatically substituted epoxy-*o*-quinols *(2)*; the aliphatically substituted 2,4,6-tri-*tert*-butyl-4,5-epoxy-6-hydroxy-2-cyclohexenone[2] yields 2,4,5-tri-*tert*-butyl-3-hydroxy-2-cyclopentenone[3].

Experimental:

(3a) from *(1a)*: O_2 is bubbled through a solution of 2 mmol *(1a)* in 10 ml tBuOH containing 5 mmol tBuOK at 75°C. The reaction mixture immediately turns orange-red; after 30 min reaction is complete. After removal of solvent and treatment with aqueous NH_4Cl solution *(3a)* is obtained in almost quantitative yield; orange-red prisms (from methanol).

(3b)—(3h): Procedure analogous to that for *(3a)*: Reaction time 1 h. The reaction mixture is poured into an excess of aqueous NH_4Cl solution, extracted with petroleum ether, and separated on silica gel with petroleum ether/CH_2Cl_2 (9:1) from the epoxy-*o*-quinols *(2)* that are also present.

(2a) from *(1a)*: O_2 is bubbled through a solution of 16 mmol *(1a)* and 67 mmol tBuOK in 100 ml tBuOH/pet. ether (1:1) at 0°C for 3h and the solution finally neutralized with aqueous NH_4Cl: 55% *(2a)*, pale yellow prisms (from petroleum ether), m.p. 95—97°C, along with 25% *(3a)*.

(3a) and *(3b)* from *(2a)* and *(2b)*, resp.: N_2 is passed through the solution of 0.2 mmol *(2a)* or *(2b)* and 0.5 mmol tBuOK im 1 ml tBuOH at 75°C. The yields of *(3a)* and *(3b)* determined by NMR spectroscopy after 30 min and 14 h, respectively, were 99% *(3a)* and 70% *(3b)*.

Table 1. Cyclopentadienones *(3)* by oxygenation of 4-aryl-2,6-di-*tert*-butylphenols *(1)* at 75°C. Yields refer to isolated products (orange needles or prisms from methanol).

	(3)	Yield [%]		M.p. [°C]	IR (CCl_4) [cm^{-1}] [a]	^{1}H-NMR ($CDCl_3$) δ [ppm]				UV/VIS (cyclohexane)
	R	1 h	6 h			tBu	Me	4-H	Ar	λ_{max} [nm] (ε)
a [b]	4-OMe	97 [c]		80—81	1709	1.10, 1.17	3.83	6.30	6.8—7.4	417 (744)
b [d]	3-OMe	20	44	89—90	1709	1.09, 1.17	3.82	6.29	6.7—7.5	413 (565)
c	2-OMe	29	40	61—62	1712	1.07, 1.17	3.84	6.27	6.7—7.5	410 (562)
d	4-Me	53	59	97—98	1712	1.09, 1.16	2.37	6.27	7.14	414 (656)
e	3-Me	27	48	98—99	1709	1.10, 1.17	2.40	6.34	6.9—7.5	413 (565)
f	2-Me	9	20	87—88	1711	1.04, 1.17	2.30	6.23	7.0—7.4	410 (516)
g	H	22	50	97—98	1714	1.07, 1.16	—	6.29	7.2—7.4	414 (523)
h	4-Cl	27		100—101	1713	1.08, 1.17	—	6.29	7.1—7.5	414 (586)

[a] Limit of error ±5 cm^{-1}. [b] Yield 99% starting from *(2a)* (30 min). [c] After 30 min. [d] Yield 70% starting from *(2b)* (14 h).

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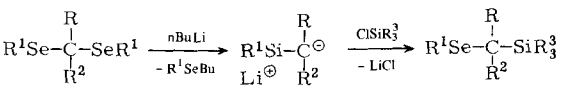
CAS Registry numbers:
(1a), 6257-22-3; *(1b)*, 6257-21-2; *(1c)*, 6257-41-6; *(1d)*, 6257-38-1; *(1e)*, 6257-37-0; *(1f)*, 6152-15-4; *(1g)*, 2668-47-5; *(1h)*, 20031-1-73-6; *(2a)*, 58282-04-5; *(2b)*, 58282-05-6; *(3a)*, 58282-06-7; *(3b)*, 58281-53-1; *(3c)*, 58281-54-2; *(3d)*, 58281-55-3; *(3e)*, 58281-56-4; *(3f)*, 58281-57-5; *(3g)*, 58281-58-6; *(3h)*, 58281-59-7; *(4a)*, 58281-60-0; *t*-BuOK, 865-47-4

[1] *A. Nishinaga, T. Itahara,* and *T. Matsuura,* Chem. Lett. *1974*, 667.
[2] *A. Nishinaga, T. Itahara,* and *T. Matsuura,* Tetrahedron Lett. *1974*, 4481.
[3] *A. Nishinaga, T. Itahara,* and *T. Matsuura,* unpublished work.

Synthesis of Olefins from α-Silyl Carbanions and Carbonyl Compounds[1]

By *Willy Dumont* and *Alain Krief*[*]

We report here on a method for the synthesis of olefins from monosubstituted α-silyl carbanions *(2)* and carbonyl compounds. This work illustrates another example of C—Se bond cleavage by *n*-butyllithium as a new methodology for the synthesis of carbanions, especially for those not accessible by classical procedures[2].



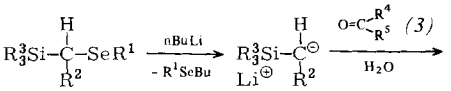
(1)

Table 1. Synthesis of methyl and phenyl α-silylmethyl selenides *(1)*.

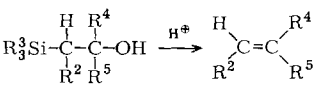
	R	R^1	R^2	R^3	Yield [%] [a]
(1a)	H	CH_3	CH_3	C_2H_5	80
(1b)	H	CH_3	C_6H_{13}	C_2H_5	91
(1c)	H	CH_3	C_6H_{13}	CH_3	85
(1d)	H	C_6H_5	C_6H_{13}	CH_3	51
(1e)	CH_3	CH_3	CH_3	C_2H_5	91

[a] Yield of purified compounds.

The previously described methods for the synthesis of α-silyl carbanions[3, 4] are not of very wide application.



(2)



(4) *(5)*

Table 2. Synthesis of β-hydroxyalkylsilanes *(4)* and olefins *(5)*. $R^1 = CH_3$.

	R^2	R^3	R^4	R^5	Yield [%] [a] *(4)*	Yield [%] [a] *(5)*
a	C_6H_{13}	CH_3	H	C_6H_{13}	50	90 [b]
b	C_6H_{13}	CH_3	C_2H_5	C_2H_5	—	40 [c]
c	C_6H_{13}	CH_3	$-(CH_2)_5-$		—	40 [c]
d	C_6H_{13}	C_2H_5	H	C_6H_{13}	30	90 [b]
e	C_6H_{13}	C_2H_5	$-(CH_2)_5-$		30	90 [b]
f	CH_3	C_2H_5	C_6H_5	$CH_2C_6H_5$	20 [d]	90 [b]
g	CH_3	C_2H_5	$-(CH_2)_2-CH(t\text{-}Bu)-(CH_2)_2-$		—	40 [c]
h	CH_3	C_2H_5	H	$C_{10}H_{21}$	—	45 [c]

[a] Yield of purified compounds. [b] Referred to *(4)*. [c] Referred to *(3)*. [d] Cf. Ref. [6].

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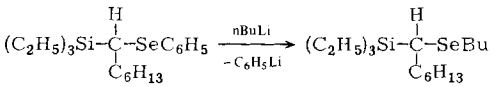
We have now found that monosubstituted methyl α-silylmethyl selenides *(1a)*—*(1c)*[5] can be cleaved up to 0 °C by *n*-butyllithium (THF, 1 h, 0 °C). The resulting carbanions *(2)* can react with carbonyl compounds *(3)* to give β-hydroxyalkylsilanes *(4)*[6], which are then transformed into olefins *(5)* in excellent yields by known procedures[7].

An interesting feature is the formation of the olefin *(5a)* (40% yield)[6] from deoxybenzoin and ethyl-1-(triethylsilyl) carbanion; this olefin is obtained in very low yield (≈10%) when ethylidenetriphenylphosphorane is reacted with the same ketone.



(1d) *(6)*

In the case of the phenyl selenide derivative *(1d)* only phenyl-Se bond cleavage is observed; butyl α-silyl selenide *(6)* is formed in 60% yield. (Phenyl lithium is trapped by its reaction with carbonyl compounds when the latter are added.)

The highly substituted methyl α-silylmethyl selenide *(1e)* is more difficult to react with *n*-butyllithium (THF, 3 h, 20 °C); some butyl methyl selenide is indeed formed but, as yet, we do not have any evidence of the formation of a carbanion of type *(2)* (with CH_3 instead of H).

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CAS Registry numbers:
n-Butyllithium, 109-72-8; *(1a)*, 58312-85-9; *(1b)*, 58312-86-0; *(1c)*, 58312-87-1; *(1d)*, 58312-88-2; *(1e)*, 58312-99-5; *(2a)*, 58312-89-3; *(2b)*, 58312-90-6; *(2c)*, 58312-91-7; *(3a)*, 111-71-7; *(3b)*, 96-22-0; *(3c)*, 108-94-1; *(3f)*, 451-40-1; *(3g)*, 98-53-3; *(3h)*, 112-44-7; *(4a)*, 58312-92-8; *(4d)*, 58312-93-9; *(4e)*, 58312-94-0; *(4f)*, 58312-95-1; *(5a)*, 10374-74-0; *(5b)*, 58312-96-2; *(5c)*, 58312-97-3; *(5f)*, 5551-45-1; *(5g)*, 14033-64-8; *(5h)*, 19150-20-0; *(6)*, 58312-98-4

[1] Part of this work was presented by the authors at the 25th IUPAC Congress held in Jerusalem (Israel), July 1975.
[2] *W. Dumont, P. Bayet,* and *A. Krief,* Angew. Chem. *86*, 857 (1974); Angew. Chem. Int. Ed. Engl. *13*, 804 (1974); *D. Seebach* and *A. K. Beck,* Angew. Chem. *86*, 859 (1974); Angew. Chem. Int. Ed. Engl. *13*, 806 (1974) and references cited therein; *A. Anciaux, A. Eman, W. Dumont,* and *A. Krief,* Tetrahedron Lett. *1975*, 1617; *D. Van Ende, W. Dumont,* and *A. Krief,* Angew. Chem. *87*, 709 (1975); Angew. Chem. Int. Ed. Engl. *14*, 700 (1975) and references cited therein.
[3] *D. J. Peterson,* J. Org. Chem. *33*, 780 (1968); *A. G. Brook, J. M. Duff,* and *D. G. Anderson,* Can. J. Chem. *48*, 561 (1970).
[4] *T. H. Chan* and *E. Chang,* J. Org. Chem. *39*, 3264 (1974); *G. R. Buell, R. Corriu, C. Guerin,* and *L. Spialter,* J. Am. Chem. Soc. *92*, 7224 (1970); *L. F. Cason* and *H. G. Brooks, ibid. 74*, 4582 (1952); J. Org. Chem. *19*, 1278 (1954).
[5] *A. Anciaux, A. Eman, W. Dumont, D. Van Ende,* and *A. Krief,* Tetrahedron Lett. *1975*, 1613.
[6] The yield of *(4)* was greatly improved when the carbonyl compound *(3)* was added to the carbanion *(2)* at −78 °C (45% instead of 20% for *(5f)*).
[7] *P. F. Hudrlik* and *D. Peterson,* J. Am. Chem. Soc. *97*, 1464 (1975).

$Ge_4S_6Br_4$—The First Sulfide Halide of Germanium[**]

By *Siegfried Pohl*[*]

Although sulfide halides of silicon have been known for some time[1] in the form of 1,3,2,4-dithiadisiletanes and their polycyclic oligomers no defined sulfide halides of germanium[2] or tin have so far been reported. A compound of the composition $Ge_4S_6Br_4$ has now been isolated by reaction of $GeBr_4$ with H_2S in carbon disulfide.

$$4\ GeBr_4 + 6\ H_2S \xrightarrow[AlBr_3]{CS_2} Ge_4S_6Br_4 + 12\ HBr$$

(1)

The almost colorless product *(1)*, m.p. 305°C (dec.), is stable in air. The difficultly crystallizable compound is only attacked by water on warming and dissolves with decomposition in caustic alkali.

A complete X-ray structure analysis shows that tetragermanium hexasulfide tetrabromide crystallizes triclinically in the space group $P\bar{1}$ with lattice constants: $a=8.806$, $b=9.940$, $c=10.104$ Å; $\alpha=86.04$, $\beta=64.08$, $\gamma=89.82°$; $V=793$ Å^3; $Z=2$. Refinement of 2228 observed reflections (single crystal data measured on a four circle diffractometer) converged to an unweighted R value of 8.7 % (without absorption correction). The molecule of *(1)* proves to have an adamantane-like structure (cf. Fig. 1). The deviations from T_d symmetry in the solid state are significant.

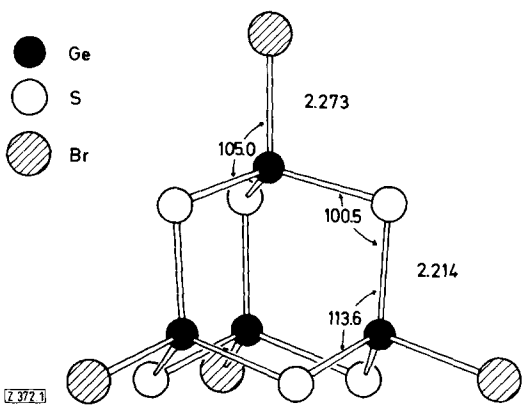

Fig. 1. Molecular structure of $Ge_4S_6Br_4$ in the solid state with mean bond lengths [Å] and angles [°].

The mean values of the lengths of chemically equivalent bonds and of some of the bond angles are given in Fig. 1. The maximum deviations of these mean values are ±0.027 Å for the Ge—S distance and ±0.010 Å for the Ge—Br distance; hence, all bond lengths lie in the range expected for Ge—S (cf. *e.g.* Ref. [3]) and Ge—Br single bonds[4].

In the Raman spectrum of solid *(1)* [70 (6), 106 (3.5), 110 (3.5), 124 (9), 126 (sh), 150 (10), 188 (2), 192 (3.5), 334 (4), 363 (8), 369 (3), 419 (1) cm^{-1} (estimated intensities from 0—10)] the peak at 363 cm^{-1} can be assigned to the symmetrical vibration of the Ge_4S_6 cage, the peaks at 192 and 188 cm^{-1} to the symmetrical Ge—Br stretching vibration.

In the FIR spectrum [73 (5), 185 (9), 300 (10), 365 (7), 380 (6), 420 (10) cm^{-1} (estimated intensities from 0—10); Nujol suspension] the two strongest bands at 420 and 300 cm^{-1} correspond to the asymmetric Ge—S and Ge—Br stretching vibrations, respectively.

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It should also be possible to prepare a series of other sulfide halides of germanium(IV) and of tin(IV) using the same synthetic principle as that for *(1)*. Indeed, we have already isolated a germanium sulfide iodide[5], which probably has the same structure as that of *(1)*. Moreover, the previously difficultly isolable thioacids[6] and thiooxo compounds[7] of germanium and tin ought to be preparatively easily accessible *via* the corresponding sulfide halides.

Experimental:

H_2S is passed for 72 h into a boiling solution of $GeBr_4$ (20 g, 50 mmol) in CS_2 (250 ml; containing catalytic amounts of $AlBr_3$) in a two-necked flask fitted with gas inlet tube and multiple coil condenser, the solvent being repeatedly replaced during the reaction. The solvent is finally removed, unreacted $GeBr_4$ distilled off, and the glassy residue dissolved in CS_2. After 4—5 d at −10°C the filtered pale yellow solution starts to crystallize; crystallization is very slow, and on completion affords 6.5 g (65 %) of *(1)*. Attempts to accelerate the crystallization by strong concentration of the solution have always resulted in a predominantly amorphous product.

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German version: Angew. Chem. *88*, 162 (1976)

CAS Registry numbers:
$GeBr_4$, 13450-92-5; H_2S, 7783-06-4; $Ge_4S_6Br_4$, 58356-00-6

[1] *A. Haas*, Angew. Chem. *77*, 1066 (1965); Angew. Chem. Int. Ed. Engl. *4*, 1014 (1965); and literature cited therein.
[2] Only a glassy, not fully characterized phase of approximate composition $GeSI_2$ has previously been described: *S. A. Dembrovskii, V. V. Kirilenko,* and *Y. A. Buslaev*, Izv. Akad. Nauk SSSR Neorg. Mater. *7*, 328 (1971).
[3] *B. Krebs, S. Pohl,* and *W. Schiwy*, Z. Anorg. Allg. Chem. *393*, 241 (1972); and literature cited therein.
[4] *M. Lister* and *L. E. Sutton*, Trans. Faraday Soc. *37*, 393 (1941).
[5] *S. Pohl* and *B. Krebs*, unpublished.
[6] The only previously reported thio acid of the two elements was described as $H_2Ge_2S_5$ but not characterized in detail: *H. H. Willard* and *C. W. Zuehlke*, J. Am. Chem. Soc. *65*, 1887 (1943).
[7] A thiooxo compound has been isolated only in the case of tin: *W. Schiwy* and *B. Krebs*, Angew. Chem. *87*, 451 (1975); Angew. Chem. Int. Ed. Engl. *14*, 436 (1975).

Tetracarbonylcobaltiopentacarbonylmanganiomercury, $(CO)_4Co—Hg—Mn(CO)_5$

By *Manfred Zöller* and *M. L. Ziegler*[*]

Compounds of mercury, cadmium, or zinc of the type Mm_2 (m = carbonylmetal group, *e.g.* $Co(CO)_4$, $Mn(CO)_5$) containing metal-metal bonds have been known for some time[1]. Corresponding unsymmetrical species mMm′ have hitherto only been accessible in cases where the carbonylmetal substituent m′ also contains an η-cyclopentadienyl ligand (*e.g.* η-$C_5H_5Fe(CO)_2$—Cd—$Co(CO)_4$)[2]. On reaction of $Mn(CO)_5Br$ with $NaCo(CO)_4$ in the presence of mercury we found evidence that very small amounts of $(CO)_4CoHgMn(CO)_5$ *(1)* are formed alongside $MnCo(CO)_9$. A better entry to this compound was found in the exchange reaction:

$$Hg[Mn(CO)_5]_2 + Hg[Co(CO)_4]_2 \rightleftharpoons 2\ (CO)_4Co—Hg—Mn(CO)_5 \quad (a)$$

(1)

Attempts to prepare the homologous zinc and cadmium compounds have so far remained unsuccessful.

Evidence for the equilibrium (a) is provided by two-dimensional layer chromatography: application of analytically pure

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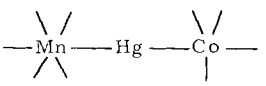
(1) to a DC plate followed by development of a normal chromatogram leads to only one zone; chromatography perpendicular to the original direction of migration after about 15 min affords not only *(1)* but also $Hg[Mn(CO)_5]_2$ and $Hg[Co(CO)_4]_2$ as separate zones.

The composition of *(1)* is confirmed by elemental analysis and the mass spectrum (rel. molecular mass 567.7987 (4.6 ppm)). The IR spectrum (*n*-pentane) contains six bands in the ν_{CO} region. Assuming free rotation about the manganese-mercury and the cobalt-mercury bond in solution, the symmetry of the "fragments" $Mn(CO)_5$ and $Co(CO)_4$, respectively, will apply, *i.e.*, for



C_{4v} ($Mn(CO)_5$) and C_{3v} ($Co(CO)_4$) point symmetry with three IR active CO stretching vibrations each ($2A_1+1E$, and $2A_1+1E$), in accord with the observed spectrum. The trigonal bipyramidal arrangement at the cobalt atom is also reasonable in the light of the results of an X-ray structure analysis of η-$C_5H_5Fe(CO)_2$—Hg—$Co(CO)_4$[2].

Procedure:

$Mn_2Hg(CO)_{10}$ (296 mg, 0.5 mmol) and $Co_2Hg(CO)_8$ (272 mg, 0.5 mmol) are stirred for 12 h in boiling acetone under N_2. After all the $Mn_2Hg(CO)_{10}$ has dissolved a deepening of color from yellow to orange takes place. The filtered solution is evaporated to dryness and the orange residue extracted with cyclohexane (30 ml), leaving unreacted $Mn_2Hg(CO)_{10}$ as residue. Separation of *(1)* and $Co_2Hg(CO)_8$ is accomplished by preparative layer chromatography under N_2 (silica gel PF_{254}, cyclohexane, layer thickness 1 mm): the first zone ($R_F=2.85$) contains unreacted $Co_2Hg(CO)_8$, and the second one ($R_F=1.61$) product *(1)*.—The second zone is cut out and *(1)* dissolved out by acetone (30 ml). The solution is evaporated at 0 °C under water pump vacuum, and the residue taken up in acetone (1 ml) and *n*-pentane (4 ml). At −18 °C this solution precipitates pale yellow crystals [yield 40 mg (14 %); m.p. 115 °C (dec.); IR data (ν_{CO} in cm^{-1}): 2098 w, 2075 sh, 2061 s, 2002 vs, 1998 vs, 1979 m].—All manipulations must be performed rapidly and under nitrogen since *(1)* undergoes significant dismutation to the symmetrical starting compounds within 1 h at room temperature.

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revised: December 22, 1975 [Z 373 IE]
German version: Angew. Chem. *88*, 188 (1976)

CAS Registry numbers:
$Hg[Mn(CO)_5]_2$, 15525-07-2; $Hg[Co(CO)_4]_2$, 13964-88-0;
$(CO)_4CoHgMn(CO)_5$, 58448-93-4

[1] *W. Hieber, E. O. Fischer,* and *E. Böckly*, Z. Anorg. Allg. Chem. *69*, 309 (1952).
[2] *R. F. Bryan* and *H. P. Weber*, Acta Crystallogr. *21*, A 138 (1966).

Use of Crosslinked Poly(4-vinylpyridine) as HCl Acceptor[**]

By *Manfred L. Hallensleben* and *Hellmuth Wurm*[*]

During the synthesis of organic compounds that are sensitive to hydrolysis the HCl liberated is usually converted into salts with tertiary amines, aniline, or pyridine which, however, cannot generally be removed quantitatively from the reaction mixture. This has an interfering effect, especially in the synthesis and purification of small amounts of substances.

Crosslinked polymers are generally insoluble in all solvents and merely swell to a greater or lesser extent. If HCl is bound to a crosslinked nitrogen base then the resulting salt[1] can readily be removed quantitatively by filtration or centrifugation from the reaction solution.

We have developed reliable methods for the synthesis of a suitable crosslinked poly(4-vinylpyridine) and its regeneration. This gel can be employed in all organic solvents, polar solvents leading to swelling of the gel and thus raising its capacity.

Crosslinked poly(4-vinylpyridine)

4-Vinylpyridine (20 g, 0.19 mol) which has been freshly distilled over KOH, technical grade divinylbenzene (1.4 g, containing *ca.* 50 % *p*-ethylvinylbenzene, remainder *m*- and *p*-divinylbenzene) which has been freshly distilled under N_2, and azoisobutyronitrile (328 mg, crystallized from ether, 0.1 mol-% based on 4-vinylpyridine) are vigorously stirred together with distilled water (750 ml). After passage of N_2 for 1 h and heating to 60 °C for 30 h in a thermostated bath, the mixture is cooled, the water poured off, and the gel extracted with methanol in a large Kutscher-Steudel extraction apparatus to remove soluble components. It is subsequently dried *in vacuo* at 64 °C; yield 17—18 g.

N-Trimethylsilylbenzamide

A solution of trimethylchlorosilane (6.6 g, 65 mmol) in dry chloroform (30 ml) is added dropwise to a vigorously stirred mixture of dry benzamide (6.7 g, 55 mmol) and crosslinked poly(4-vinylpyridine) (6.3 g, 60 mequiv.) in dry chloroform at 40 °C. Stirring is continued for 30 min and the mixture then filtered through a glass frit with exclusion of moisture. After removal of solvent essentially pure *N*-trimethylsilylbenzamide is obtained.—Regeneration of the HCl acceptor is conveniently accomplished by stirring of the gel with dilute methanolic NaOH, filtration through a Buchner funnel, washing with water and then with methanol, and finally drying *in vacuo*.

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German version: Angew. Chem. *88*, 192 (1976)

CAS Registry numbers:
Crosslinked poly(4-vinylpyridine), 58426-90-7;
N-trimethylsilylbenzamide, 1011-57-0; benzamide, 55-21-0;
trimethylchlorosilane, 75-77-4

[1] Regarding complexes of metals salts with poly(4-vinylpyridine) see *H. G. Biedermann, J. Obwandner,* and *K. Wichmann*, Z. Naturforsch. *27b*, 1332 (1972).

syn-Tricyclo[5.1.0.0^{2,4}]oct-5-ene-3,8-dicarboxylate[**]

By *Gerd Kaupp* and *Klaus Rösch*[*]

The photolysis of 1,3,6-cyclooctatriene proceeds *via* an intramolecular Diels-Alder reaction to give *anti*-bishomobenzene *(3)*[1]. In contrast, 5,8-*cis*-disubstituted 1,3,6-cyclooctatrienes should permit the synthesis of *syn*-bishomobenzenes *(4)*

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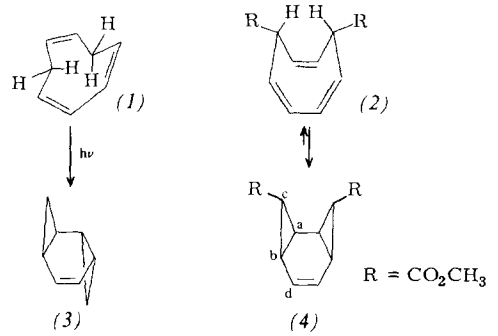
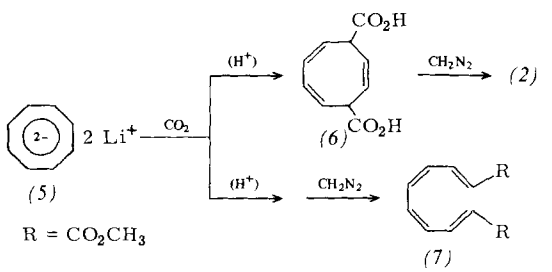
because they do not exist in a rotationally symmetrical conformation (analogous to *(1)*) for steric reasons but instead, at the expense of a transannular H/H interaction, most probably in a conformation having a symmetry plane (corresponding to *(2)*).

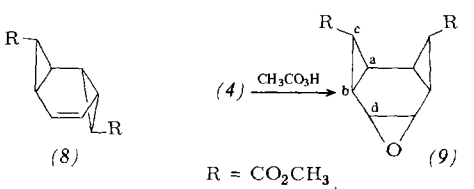


Since only heterocyclic *syn*-bishomobenzene derivatives have hitherto been synthesized[2, 3] we attempted to prepare the dicarboxylic ester *(2)* from cyclooctatetraenedilithium *(5)*, carbon dioxide, and diazomethane. To our surprise we isolated 29 % of *(4)* and 6 % of *(7)* as reaction products.

This result contradicts earlier reports that *(5)* reacts with CO_2 to give either 80 % of *(6)*[4] or (after the action of CH_2N_2) 50 to 65 % of *(7)* together with 0 to 3 % of *(2)*[5]:



The differing findings still require an explanation. The structure of *(4)* ($C_{12}H_{14}O_4$[6], m.p. 87—89 °C) follows unequivocally from a comparison with the *anti* isomer *(8)*[7], its ^{1}H-NMR spectrum [$CDCl_3$: δ = 0.7—1.0 (2 H^c, m), 1.6—2.05 (2 H^b, m), 2.05—2.4 (2 H^a, m), 3.73 (6H, s), 6.05—6.3 ppm (2 H^d, m); coupling between H^b and H^d], and epoxidization to give *(9)*[6] [m.p. 185—187 °C; NMR ($CDCl_3$): δ = 1.35—1.6 (2 H^c, m), 1.7—2.25 (4 $H^{a,b}$, m), 3.3—3.35 (2 H^d, m), 3.75 ppm (6H, s)]. For steric reasons and because of the relatively narrow NMR signal of the epoxide ring protons the *syn/anti* structure is assigned to *(9)*. It is formed from *(4)* and peracetic acid in methylene chloride in the presence of solid disodium hydrogen phosphate (24 h stirring at *ca.* 25 °C; 84 % yield after crystallization from benzene).



The crystals of the readily accessible *syn*-bishomobenzene derivative *(4)* can be stored for several days at room temperature. In solution it equilibrates within a few hours with *ca.* 20 % of *(2)* at room temperature [NMR ($CDCl_3$): δ = 3.76 (6H, s), 4.15—4.4 (2H, br. t, J = 5.1 Hz), 5.7—6.1 ppm (6H, m)]. On heating to 60 °C for half an hour the proportion of *(2)* increases but irreversible reactions then also compete.

The possibility of virtually unhindered attack at the double bond endows *(4)* with considerable potential as a synthetic reagent.

Dimethyl syn-tricyclo[5.1.0.0^{2,4}]oct-5-ene-3,8-dicarboxylate (4):

A solution of *(5)*[4, 5], prepared from cyclooctatetraene (15.5 g) and lithium (2.1 g) in diethyl ether/tetrahydrofuran (9 : 1, 500 ml) under argon, is poured on to dry ice (*ca.* 500 g) in a stream of inert gas (danger of ignition!). After addition of ether (100 ml) and (at room temperature) water (200 ml) and conc. HCl (60 ml) the mixture is filtered under suction from 7.0 g of precipitate (yielding 1.0 g of *(7)* with CH_2N_2). Treatment with a further portion of conc. HCl (40 ml) affords 19.9 g of residue after extraction with ether (2 l) and evaporation, of which 11.4 g dissolve in 250 ml of ether at 25 °C (affording 0.8 g of *(7)* and 1.0 g of *(4)* on esterification and chromatography). On treatment with diazomethane in methanol/ether and chromatography over SiO_2 with CH_2Cl_2 the remainder gives 8.7 g of *(4)*, which is recrystallized from CH_3OH at −20 °C.

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(1), 3725-30-2; *(2)*, 58343-25-2; *(3)*, 3786-99-0; *(4)*, 58383-69-0; *(5)*, 34728-91-1; *(6)*, 58343-26-3; *(7)*, 38127-08-1; *(8)*, 35242-13-8; *(9)*, 58383-70-3

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[2] *H. Prinzbach, M. Breuninger, B. Gallenkamp, R. Schwesinger*, and *D. Hunkler*, Angew. Chem. *87*, 350 (1975); Angew. Chem. Int. Ed. Engl. *14*, 348 (1975).

[3] *E. Vogel, H. J. Altenbach*, and *D. Cremer*, Angew. Chem. *84*, 983 (1972); Angew. Chem. Int. Ed. Engl. *11*, 935 (1972); *H. J. Altenbach* and *E. Vogel, ibid. 84*, 985 (1972) and *11*, 937 (1972), respectively; *E. Vogel, E. Schmidbauer*, and *H. J. Altenbach, ibid. 86*, 818 (1974) and *13*, 736 (1974); *D. Stusche, M. Breuninger*, and *H. Prinzbach*, Helv. Chim. Acta *55*, 2359 (1972).

[4] *W. Reppe, O. Schlichting, K. Klager*, and *T. Toepel*, Justus Liebigs Ann. Chem. *560*, 1 (1948).

[5] *T. S. Cantrell*, Tetrahedron Lett. *1968*, 5635; J. Am. Chem. Soc. *92*, 5480 (1970).

[6] All new compounds gave correct values on elemental analysis. NMR assignments are confirmed by selectively decoupled ^{13}C-NMR spectra [*(4)* ($CDCl_3$): δ = 173.2 (s), 125.1 (d), 51.9 (q), 28.4 (d), 19.5 (d), 16.9 ppm (d)].

[7] *D. L. Dalrymple* and *S. P. B. Taylor*, J. Am. Chem. Soc. *93*, 7098 (1971).

$Mn_2(CO)_{10}CH_2N_2$, A Stable Organometallic Derivative of Diazomethane[1]

By *W. A. Herrmann, M. L. Ziegler, K. Weidenhammer, H. Biersack, K. K. Mayer*, and *R. D. Minard*[*]

Intermediate diazomethane- and carbene complexes are responsible for the variety of reactions diazomethane exhibits in the presence of catalytically active metal compounds[2]. It was recently shown that carbene, CH_2, could be transferred

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from its diazo precursor to organometallic compounds[3]. We now report the introduction of unfragmented diazomethane, CH_2N_2, into a manganese complex with an unusual structure.

Reaction of pentacarbonyl manganese hydride in tetrahydrofuran at −85 °C with excess diazomethane and subsequent column chromatography at room temperature afforded a light yellow, easily crystallized, air stable and thermally stable (*ca.* 115 °C dec.) compound[4]. From the complete elemental analysis and high resolution mass spectrum it follows that the diamagnetic compound formed according to

$$2\ Mn(CO)_5H + CH_2N_2 \xrightarrow[-H_2]{THF/-85\,^\circ C} Mn_2(CO)_{10}CH_2N_2 \quad (1)$$

has the empirical formula $C_{11}H_2Mn_2N_2O_{10}$; the osmometric molecular weight determination also confirms the presence of a binuclear neutral compound *(1)*. The carbene insertion product $(CO)_5MnCH_3$ discovered by *Hieber et al.*[5] was not found in the final product under our experimental conditions.

On electron impact ionization of *(1)* in the mass spectrometer (Varian MAT CH 5; $P_E = 70$ eV; Em = 300 μA; $T_Q = 80$ °C; direct inlet $T = 50$ °C) the molecular ion ($m/e = 432$) successively loses ten CO groups, with the base peak at $[M-9CO]^+$ ($m/e = 180$); further decomposition of $Mn_2CH_2N_2^+$ proceeds *via* $MnCH_2N_2^+$ to $MnCH_2^+$ ($m/e = 69$, rel. int. 52 %). Besides the $Mn_2(CO)_{10}CH_2N_2$ series a decay series of mononuclear ions starting from $(CO)_5MnCH_2N_2^+$ ($m/e = 237$) is also observed.

Although the mass spectrometric high resolution analysis of the parent and the fragment ions proved incorporation of intact diazomethane in the complex molecule, no proton signals could be detected in the ^{1}H-NMR spectrum. In order to clarify this dichotomy we carried out a complete three dimensional X-ray structure analysis of *(1)*[6]. It showed that diazomethane has, indeed, been introduced as an unfragmented species into a binuclear complex consisting of both $Mn(CO)_5$- and $Mn(CO)_4$-moieties (Fig. 1). *(1)* is part of an unusual four-membered framework arising from conversion of a terminal carbonyl group into an acyl function. The bridging system is coplanar including both hydrogen atoms localized by X-ray analysis.

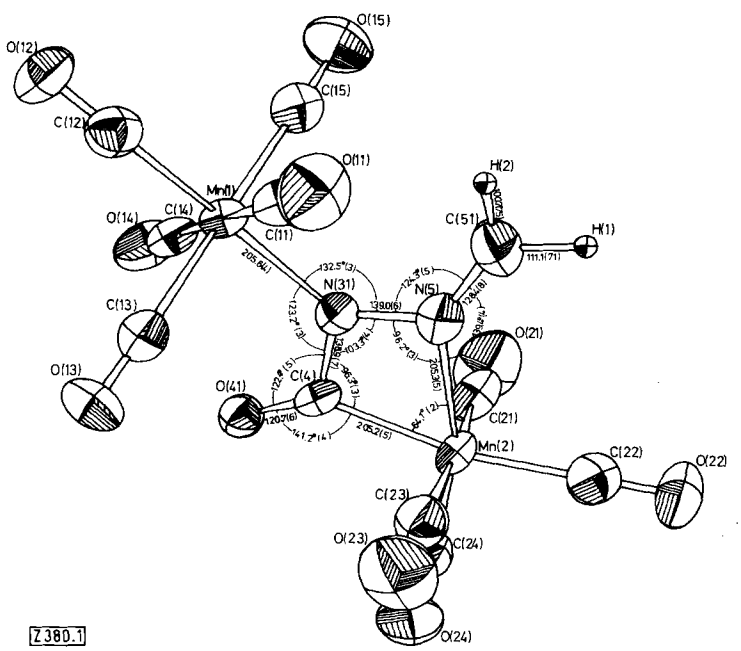

Fig. 1. ORTEP plot of the molecular structure of *(1)*. The thermal ellipsoids have 50 % probability; all atoms are drawn in proper dimensions except for hydrogen (bond lengths in pm).

The IR spectra of *(1)* can also be interpreted on the basis of these structural data: The intense bands at 1644 and 1575 cm^{-1} (KBr) are assigned to the ketonic CO and the N=CH_2-groups, respectively. From the nine possible IR active valence vibrations (7A′+2A″) of the terminal CO groups postulated by a vibration analysis for a molecule of symmetry C_s, eight are observed as separate bands (2122 w, 2086 m, 2062 vw, 2036 vs, 2027 vs, 2005 s-vs, 1988 vs, and 1966 cm^{-1} vs; cyclohexane).

The synthesis of *(1)* is the first example of coordination of diazomethane to metal *via* both nitrogen atoms. Our results demonstrate that the basicity of the diazo carbon atom is not necessarily the key function for the special reactivity of diazomethane toward metal compounds. The initial reactions can also occur exclusively at the diazo group if the metal complex fulfills chemical and structural requirements.

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CAS Registry numbers:
$Mn(CO)_5H$, 16972-33-1; CH_2N_2, 334-88-3; $Mn_2(CO)_{10}CH_2N_2$, 58448-92-3

[1] Complex Chemistry of Reactive Organic Compounds, Part 11.—Part 10: *W. A. Herrmann*, Chem. Ber. *108*, 3412 (1975).
[2] *M. F. Lappert* and *J. S. Poland*, Adv. Organometal. Chem. 9, 397 (1970); *P. W. Jolly* and *G. Wilke*, The Organic Chemistry of Nickel, Vol. I, Academic Press, New York 1974.
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[4] In addition, three other new complexes could be isolated and identified by elemental analyses, spectroscopic investigations, and X-ray analyses. *W. A. Herrmann*, *M. L. Ziegler*, and *K. Weidenhammer*, to be published.
[5] *W. Hieber* and *G. Wagner*, Z. Naturforsch. *12b*, 478 (1957); Justus Liebigs Ann. Chem. *618*, 24 (1958); DBP 1053504 (1959), BASF; Chem. Abstr. 55, 9282 (1961).
[6] The compound crystallizes from methylene chloride/acetone (1 : 1; −35 °C) monoclinically in the space group C_{2h}^5-$P2_1/c$ with $a = 1052.6(3)$, $b = 1062.0(1)$, $c = 1429.5(7)$ pm, $\beta = 93.62(5)°$, $Z = 4$. 2932 independent non-zero reflections were recorded with an automatic Siemens single crystal diffractometer (AED) and corrected in the usual manner: $R = 4.6$ %.

Cyclopropanation of [2.2]Paracyclophanes[1]

By *Klaus Menke* and *Henning Hopf*[*]

As X-ray structure analysis shows[2], in [2.2]paracyclophane-1,9-diene, and presumably also in the parent hydrocarbon [2.2]paracyclophane *(1)*[3], the aromatic hydrogen atoms do not lie in the plane of the benzene rings but are bent toward the hydrogens of the opposite benzene ring. This unusual structural feature is ascribed to a partial rehybridization of the benzene carbon atoms ($sp^2 \rightarrow sp^3$). A consequence is that part of the π-electron density is shifted to the outside faces of the molecule and the energetically unfavorable transannular penetration of the π-systems of the two benzene rings pressed face-to-face is reduced[3]. As a result of this increased external electron density, *(1)* and its derivatives ought to readily undergo addition reactions with divalent species–carbenes, nitrenes, and possibly oxygen in the case of epoxidation. The cyclopropanation of tetramethyl [2.2]paracyclophane-4,5,12,13-tetracarboxylate *(2)* described here confirms this assumption.

(2) reacts already at 10–15 °C with a 40-fold excess of diazomethane[4] in dichloromethane in the presence of cataly-

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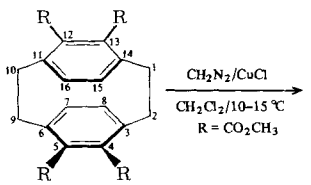
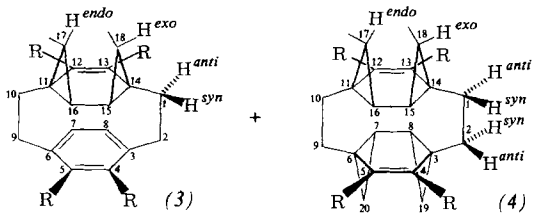
tic amounts of copper(I) chloride to give a mixture of products, which according to the nuclear resonance spectrum and mass spectrum contains some starting material along with predominant amounts of mono- to tetra adducts as well as traces of penta- to octa adducts of methylene and *(2)*. By column chromatographic separation of the mixture on neutral silica gel (Merck, Type 60; benzene/ethyl acetate = 9:1 v/v) and multiple crystallization from benzene the diadduct *(3)* (rel. mol. wt. according to the mass spectrum, 468, 7.9%; m.p. 194–196 °C) and the tetradduct *(4)* (rel. mol. wt. 496, 6.6%; m.p. 225–228 °C) could be isolated in analytically pure form. The structural assignments follow from the spectral data (Table 1)[5,6]



(1), R = H
(2), R = CO_2CH_3



(3) *(4)*

as intermediate, are hetero *cis*-bishomobenzenes, whose stability is presumably due to the presence of nitrogen[9], oxygen[10], or sulfur atoms[11] in the three-membered rings.

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(1), 1633-22-3; *(2)*, 37437-90-4; *(3)*, 58281-97-3; *(4)*, 58281-98-4; *(5)*, 58342-05-5; *(6)*, 58281-99-5; diazomethane, 334-88-3

[1] Cyclophanes, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. – Part 2: *H. Hopf* and *F. Th. Lenich*, Chem. Ber. *107*, 1891 (1974).
[2] *C. L. Coulter* and *K. N. Trueblood*, Acta Crystallogr. *16*, 667 (1963).
[3] *D. J. Cram* and *J. M. Cram*, Acc. Chem. Res. *4*, 204 (1971).
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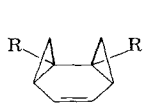
[5] We thank Dr. *R. Ader* (Chemistry Department, Technion, Israel Institute of Technology, Haifa, Israel) and Dr. *Ch. Brown* (University Chemistry Laboratory, University of Kent, Canterbury, England) for the ^{13}C-NMR spectra.
[6] *Note added in proof* (February 8, 1976): In the meantime the mono- and triadducts have also been characterized. These compounds are stable norcaradienes. The monocyclopropanated tetraester rearranges on warming (70 °C) to give the "cycloheptatrienophene"; cf. *R. Näder* and *A. de Meijere*, Angew. Chem. *88*, 153 (1976); Angew. Chem. Int. Ed. Engl. *15*, 166 (1976).
[7] For a review see: Nachr. Chem. Tech. *20*, 188 (1972).
[8] *H. W. Whitlock, Jr.* and *P. F. Schatz*, J. Am. Chem. Soc. *93*, 3837 (1971).
[9] *B. Stusche, M. Breuninger*, and *H. Prinzbach*, Helv. Chim. Acta *55*, 2359 (1972).
[10] *H.-J. Altenbach* and *E. Vogel*, Angew. Chem. *84*, 985 (1972); Angew. Chem. Int. Ed. Engl. *11*, 937 (1972).
[11] *E. Vogel, E. Schmidbauer*, and *H.-J. Altenbach*, Angew. Chem. *86*, 818 (1974); Angew. Chem. Int. Ed. Engl. *13*, 736 (1974).

Table 1. IR, UV, ^{1}H-NMR, and ^{13}C-NMR spectra of *(3)* and *(4)*.

	(3)	*(4)*
IR (KBr)	1717, 1595, 1432, 1247, 1200, 1108, 1097 (sh), 1008 cm^{-1}	1725, 1708 (sh), 1609 [a], 1430, 1248, 1220, 1093, 1014 cm^{-1}
UV (ethanol)	λ_{max} = 219 (ε = 23100) and 308 nm (1980)	λ_{max} = 244 nm (ε = 9400)
^{1}H-NMR ($CDCl_3$/int. TMS), δ values	−0.37 (2H, m, 17-, 18-H^{endo}) 0.56 (2H, m, 17-, 18-H^{exo}) 1.01–1.70 (4H, m, 1-, 10-H^{syn}, 15-, 16-H) 2.13–3.25 (6H, m, 1-, 10.H^{anti}, 2-, 9-H) 3.75 (6H, s, $-CO_2CH_3$ on C-12 and C-13) 3.87 (6H, s, $-CO_2CH_3$ on C-4 and C-5) 7.39 (2H, s, 7-, 8-H)	−0.04 (4H, m, 17- to 20-H^{endo}) 0.72 (4H, m, 17- to 20-H^{exo}) 1.08 (4H, m, 1-, 2-, 9-, 10-H^{syn}) 1.85 (4H, m, 7-, 8-, 15-, 16-H) 2.37 (4H, m, 1-, 2-, 9-, 10-H^{anti}) 3.78 (12H, s, $-CO_2CH_3$)
^{13}C-NMR ($CDCl_3$/int. TMS, band decoupled), δ values	168.30, 167.97 (C=O of the estergroups) 138.85 (C-12, C-13) 137.49, 134.44, 130.69 (C-3 to C-8) 52.23 (CH_3O- of the ester groups on C-12 and C-13) 51.72 (CH_3O- of the ester groups on C-4 and C-5) 35.54 (C-1, C-10), 30.03 (C-2, C-9) 24.27 (C-17, C-18), 18.38 (C-11, C-14), 17.02 (C-15, C-16)	169.10 (C=O of the ester groups) 138.16 (C-4, C-5, C-12, C-13) 52.06 (CH_3O- of the ester groups) 33.40 (C-1, C-2, C-9, C-10) 23.85 (C-17 to C-20) 18.33 (C-3, C-6, C-11, C-14) 17.22 (C-7, C-8, C-15, C-16)

[a] νC=C, more intense than in *(3)*.

As stable carbocyclic *cis*-bishomobenzene derivatives the esters *(3)* and *(4)* are of considerable interest[7]. Though the preparation of several derivatives of the previously



(5), R = H
(6), R = CO_2CH_3

unknown and probably very unstable parent hydrocarbon *cis*-bishomobenzene *(5)* have recently been reported the compounds mentioned here, excluding the diester *(6)*[8] detected

Methylenation of [2.2]Paracyclophane-1,9-diene and [2.2]Paracyclophane[**]

By *Reinhard Näder* and *Armin de Meijere*[*]

In [2.2]paracyclophane *(3)* the C—C σ-bond orbitals of the two bridges are parallel to the π-orbital axes of the benzene

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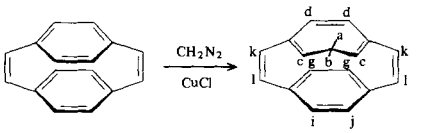
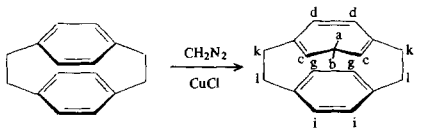
[**] This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie

rings; they thus promote interaction between the two non-conjugated benzene rings, as is revealed, for example, in the UV spectrum of *(3)*[1]. Model calculations have shown that this interaction ought to increase considerably with bridging by two cyclopropane rings[2] in the place of the ethylene bridges.

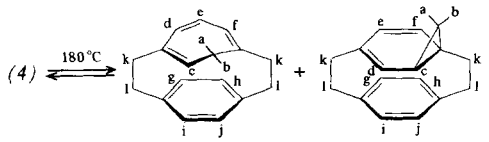
[2.2]Paracyclophane-1,9-diene *(1)*[3] appeared to us to be a suitable starting compound for the synthesis of $[0^{1,3}.0^{10,12}]$[3.3]paracyclophane, since olefinic double bonds are usually cyclopropanated much more readily than aromatic double bonds[4]. *(1)* reacts smoothly with diazomethane in the presence of copper(I) chloride. Even on reaction with



(1) *(2)*



(3) *(4)*



(5) *(6)*

small amounts of diazomethane several products were obtained, which, according to their relative molecular weights (combined GC-MS), could only be the mono-, di-, and trimethylenated derivatives of *(1)*. On further reaction the product pattern steadily changed in favor of the di-, tri-, and higher methylenated products, though *(1)* was always present in excess. Consequently, the monoadduct is more readily methylenated than the starting material. This can be rationalized only in terms of initial attack at a benzene ring and not at an olefinic double bond; because of the concomitant removal of aromaticity, this ring undergoes further reaction more rapidly than the remaining aromatic ring.

Only one monoadduct[5] has so far been isolated pure by preparative gas chromatography. According to its ^{1}H-NMR spectroscopic data (Table 1) the structure *(2)*[6] was assigned to it. Structures with a bridged norcaradiene system can be disregarded, as is immediately apparent on comparison with ^{1}H-NMR data for known norcaradiene derivatives[7]. The structure isomeric with *(2)*, and containing a 1,4-bridged cycloheptatriene ring, can be ruled out on the basis of double resonance experiments.

[2.2]Paracyclophane *(3)* reacts analogously to *(1)* with diazomethane/copper(I) chloride to give a mixture of mono-, di-, tri-, and higher methylenated products, as has been established by combined GC-MS molecular weight determinations. *(3)* reacts more slowly than *(1)*, evidently because of the less pronounced deformation of the benzene rings than in *(1)*[9].

According to its 270-MHz ^{1}H-NMR spectrum (Table 1), the monoadduct[6] which was isolated by gas chromatography and appeared to be homogeneous on several analytical GC columns, consists of the isomers *(4)*, *(5)*, and *(6)*. The assignment of structures *(4)* and *(5)* is confirmed analogously to that of *(2)* and by comparison with the ^{1}H-NMR data of cycloheptatriene[7]. The weak intensity NMR signals of H^a, H^b, and H^c and a few other signals which can neither belong to *(4)* nor to *(5)*, are consistent only with structure *(6)* containing a bridged norcaradiene system [amount of *(6)* < 10%].

The composition of the mixture of isomeric monoadducts of *(3)* depends on the column temperature during gas-chromatographic separation. A sample isolated at 140 °C contained 64% *(4)* and 36% *(5)*, whereas a sample trapped at 180 °C proved to contain 44% *(4)*, 47% *(5)*, and 9% *(6)*. While *(4)*, and possibly also *(6)*, are primary products, *(5)* can only be formed by a [1.5]-hydrogen shift from *(4)*.

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CAS Registry numbers:
(1), 6572-60-7; *(2)*, 58282-00-1; *(3)*, 1633-22-3; *(4)*, 58282-01-2; *(5)*, 58311-69-6; *(6)*, 58282-02-3; diazomethane, 334-88-3

[1] *R. Gleiter*, Tetrahedron Lett. *1969*, 4453, and literature cited therein; cf. also Angew. Chem. *86*, 770 (1974); Angew. Chem. Int. Ed. Engl. *13*, 696 (1974).
[2] *R. Gleiter*, private communication.
[3] *K. C. Dewhurst* and *D. J. Cram*, J. Am. Chem. Soc. *80*, 3115 (1958).
[4] See *e.g.*: *D. Wendisch* in Houben-Weyl: Methoden der Organischen Chemie, Thieme, Stuttgart 1971, Vol. IV/3.
[5] In one experiment, two monoadducts were detected in the reaction mixture by gas chromatography; one of these disappeared completely after storage of the reaction solution in a refrigerator for 2 days. It can only be assumed that presence of the norcaradiene tautomer of *(2)* was involved.
[6] The empirical formula of the compound was confirmed by high-resolution mass spectrometry.
[7] Cf. *G. Maier*, Angew. Chem. *79*, 446 (1967); Angew. Chem. Int. Ed. Engl. *6*, 402 (1967).
[8] We thank Dr. *E. Grell*, Max-Planck-Institut für Biophysikalische Chemie, Göttingen, for recording the 270-MHz ^{1}H-NMR spectra.
[9] *D. J. Cram* and *J. M. Cram*, Acc. Chem. Res. *4*, 204 (1971).

Table 1. 270-MHz ^{1}H-NMR data[8] of the monomethylenation products of *(1)* and *(3)*

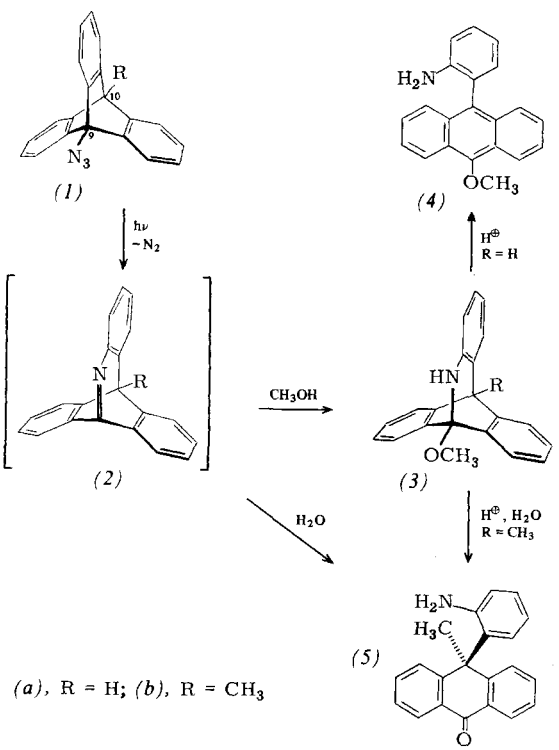
Compound / Proton	*(2)* δ [ppm]	*(2)* J [Hz]	*(4)* δ [ppm]	*(4)* J [Hz]	*(5)* δ [ppm]	*(5)* J [Hz]	*(6)* δ [ppm]
H^a	1.40	H^a–H^b: 13.1	1.34	H^a–H^b: 13.1	1.20	H^a–H^b: 12.3	0.40
H^b	2.63	H^b–H^c: 7.1	2.58	H^b–H^c: 7.7	2.21	H^b–H^c: 8.1	1.00
H^c	4.97	H^a–H^c: 6.1	4.89	H^a–H^c: 6.0	4.13	H^a–H^c: 6.5	0.92
H^d	5.53		5.56		6.06	H^d–H^e: 10.9	5.74
H^e	—		—		6.16	H^e–H^f: 5.3	5.27
H^f	—		—		5.70	H^f–H^b: 1.7	5.82
H^g	6.52	H^g–H^i: ≈1.5	6.55	H^g–H^i: 1.1	6.38	H^g–H^h: 7.6	5.99
H^h	—		—		6.54	H^h–H^i: 1.6	5.88
H^i	6.92		6.92	H^i–H^l: 1.1	6.98	H^g–H^i: 1.8	7.54
H^j	—		—		6.82	H^i–H^j: 8.0	7.72
H^k	6.55		2.96–1.73		2.96–1.73		2.96–1.73
H^l	7.13						

Photolysis of 9-Azidotriptycenes[**]

By *Helmut Quast* and *Philipp Eckert*[*]

The photolysis of 1-azidoadamantane led to formation of a strained "bridgehead imine" (the bridgehead is the C atom of the >C=N— group), whose presence was established by secondary reactions[1]. In order to check whether the solvation of the azido group plays a role in the photolysis—as assumed in the case of 1-azidonorbornane[2]—we have investigated the 9-azidotriptycenes *(1)*, in which this solvation does not occur for steric reasons. Obviously, the possible formation of the very highly strained, hypothetical "bridgehead imine" *(2)* attracted most attention.

The 9-azidotriptycenes *(1a)* and *(1b)*[3] are readily accessible by reaction of the corresponding 9-lithiotriptycenes[4] with *p*-toluenesulfonyl azide in ether and subsequent thermolysis of the resulting triazene salts in boiling benzene[5] (yield 78 and 75%, respectively, based on the 9-bromotriptycenes).

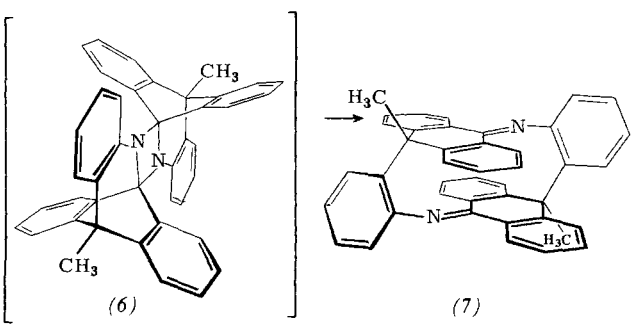


(a), R = H; *(b)*, R = CH_3

Photolysis[6] of *(1a)* and *(1b)* in methanol yielded 64 and 42%, respectively, of the azahomotriptycenes *(3)*[3], which can be regarded as adducts of the solvent to *(2)*. Whereas *(3a)* was already rapidly converted into the anthracene derivative *(4)* by trace amounts of acid in deuteriochloroform, *(3b)* was expectedly far less sensitive to acid. Only on prolonged heating in methanol/2N hydrochloric acid (4:1) was the ring opened quantitatively to the anthrone *(5)*, which by diazotization and reduction with hypophosphorous acid was converted to 10-methyl-10-phenyl-anthrone[7]. *(5)* is formed directly in 90% yield on irradiation of *(1b)* in dioxane/water (2.4:1) or *tert*-butyl alcohol. Photolysis[6] of *(1a)* in cyclohexane followed by preparative layer chromatography affords 53% of an intensely orange, yellow fluorescing product, which sublimes at 310°C/5×10^{-5} torr, decomposes at 325°C, and is formally a dimer of *(2a)*. Under the same conditions *(1b)* produces two dimers of *(2b)*. Whereas the structure of the yellow product (yield 21%, m.p. 339°C) has been elucidate[3], that of the colorless compound (yield 29%, dec. pt. 376–380°C) is still unknown.

The 270-MHz ^{1}H-NMR spectrum[8] in D_8-dioxane showed only *one* singlet (1.87 ppm) for the two methyl groups and a $(ABCD)_2$ system which could be simulated with $\delta_A = 8.040$, $\delta_B = 7.276$, $\delta_C \approx 7.124$, $\delta_D = 6.555$ ppm and $J_{AB} = 7.76$, $J_{AC} = 1.85$, $J_{AD} = 0$, $J_{BC} = 7.04$, $J_{BD} = 1.44$, $J_{CD} = 8.65$ Hz. The remaining protons gave only two remarkably broad, almost unresolved signals at 6.6 (4H) and 7.1 ppm (12H). The fact that the 42 C-atoms present showed only 15 signals in the ^{13}C-NMR spectrum (25.2 MHz, D_8-dioxane[8]) provided further evidence for a symmetric structure. The signal appearing at lowest field (151.1 ppm) and a strong IR absorption at 1648 cm^{-1} are indicative of C=N bonding and hence of a possible degradation.

The smooth hydrolytic cleavage by heating with methanol/2N hydrochloric acid finally furnished *two* mols of *(5)*, and thus confirmed structure *(7)*. However, it is still unknown whether the *trans*-configuration as depicted or a *cis*-configuration having C_2-symmetry is preferred. According to the NMR spectra rapid diastereomerization takes place already at ambient temperature.



The surprising formation of the phane structure *(7)* with a 14-membered ring can be explained by *(2b)*→*(6)*→*(7)*. The analogous *acid-catalyzed* transformation of a seven-membered cyclic imine is already known[9].

The parallel photochemical behavior of such differing bridge-head azides as 1-azidoadamantane and *(1)* indicates that solvation effects do not play a decisive role and that bridgehead azides in general are simple precursors of highly strained "bridgehead imines".

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CAS Registry numbers:
(1a), 58325-20-5; *(1b)*, 58325-21-6; *(3a)*, 58325-22-7; *(3b)*, 58325-23-8; *(4)*, 58325-24-9; *(5)*, 58325-25-0; *(7)*, 58325-26-1

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[**] Bridgehead Azides, Part 2. This work was supported by the Fonds der Chemischen Industrie. The results are planned as the subject of a doctoral thesis by Ph. E. – Part 1: Ref. [1].

[1] *H. Quast* and *Ph. Eckert*, Justus Liebigs Ann. Chem. *1974*, 1727.
[2] *J. O. Reed* and *W. Lwowski*, J. Org. Chem. *36*, 2864 (1971).
[3] The structures of all the new compounds were derived from elemental analyses, IR, UV, ^{1}H-NMR and mass spectra. In addition the empirical formulas of the "dimers" of *(2)* were confirmed by high resolution mass spectra.
[4] *G. Wittig* and *W. Tochtermann*, Justus Liebigs Ann. Chem. *660*, 23 (1962); *G. Wittig*, Acc. Chem. Res. *7*, 6 (1974).
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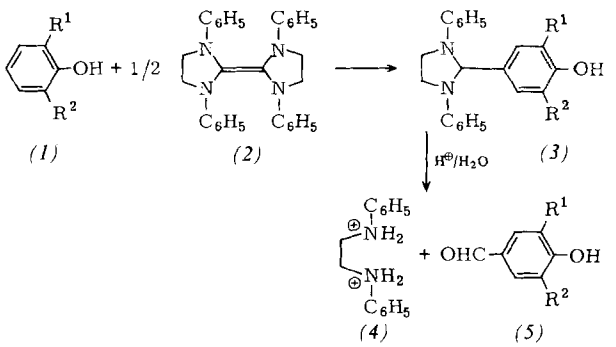
[6] Corex-filter, 450 W-Hanovia lamp, cf. [1].
[7] *C. K. Bradsher* and *D. J. Bearers*, J. Org. Chem. *21*, 1067 (1956).
[8] We thank Dr. *D. F. Hillenbrand*, University of Wisconsin, Madison, Wis. (USA), for recording these spectra.
[9] *I. M. Goldman*, *J. K. Larson*, *J. R. Tretter*, and *E. G. Andrews*, J. Am. Chem. Soc. *91*, 4941 (1969); cf. *G. Tóth*, *I. Pintér*, and *A. Messmer*, Tetrahedron Lett. *1974*, 735.

Synthesis of Phenolaldehydes with Electron-Rich Olefins[1]

By *Jürgen Hocker*, *Henning Giesecke*, and *Rudolf Merten*[*]

The methods commonly employed for the synthesis of phenolaldehydes frequently afford mixtures of *o*- and *p*-isomers in only moderate yields[2].

We have now found that cyclic aminals of phenolaldehydes *(3)* can often be obtained in good yields when phenols *(1)* are allowed to react with electron-rich olefins such as 1,1',3,3'-tetraphenyl-2,2'-biimidazolidinylidene *(2)*[3]. *(2)* is readily accessible from *N,N'*-diphenylethylenediamine and triethyl orthoformate and is easy to handle on account of its being only slightly sensitive toward oxidation. The cyclic aminal group enters preferably *para* to the phenolic OH group (Table 1).



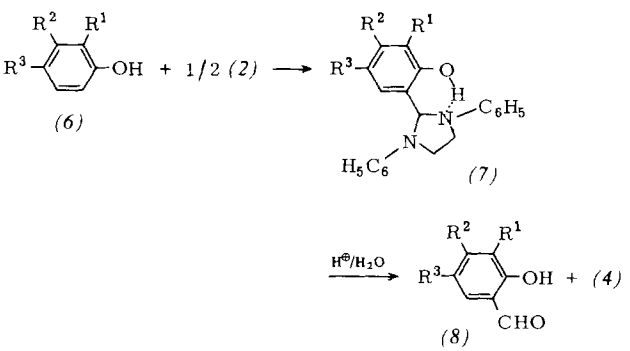
(1) *(2)* *(3)* *(4)* *(5)*

Table 1. 4-Aminals *(3)* from phenols *(1)* and 1,1',3,3'-tetraphenyl-2,2'-biimidazolidinylidene *(2)* in boiling dimethylformamide.

(3)	R^1	R^2	Yield [%]	*t* [min]
a [a]	H	H	55	10
b	CH_3	CH_3	58	15
c	*i*-C_3H_7	*i*-C_3H_7	26	15
d	*t*-C_4H_9	*t*-C_4H_9	84	15
e	CH_3	Cl	74	5
f	Cl	Cl	58	10

[a] The bis-aminal 1-(1,3-diphenyl-2-imidazolidinyl)-4-(1,3-diphenyl-2-imidazolidinyloxy)benzene is obtained, which smoothly hydrolyzes to *p*-hydroxybenzaldehyde.

If the *p*-position of the phenol is blocked or sterically hindered the reaction proceeds very selectively *via* the 2-aminals *(7)* to the salicylaldehydes *(8)* (Table 2).



(6) *(7)* *(8)*

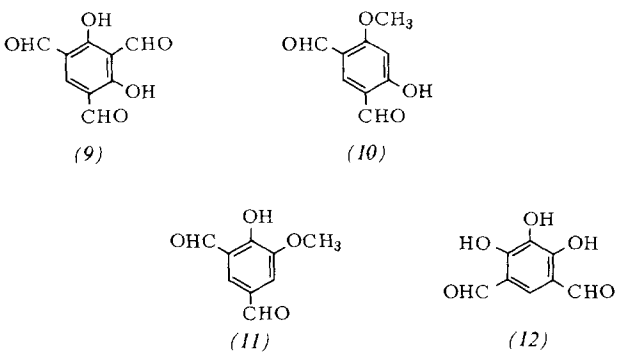
Table 2. 2-Aminals *(7)* from phenols *(6)* and 1,1',3,3'-tetraphenyl-2,2'-biimidazolidinylidene *(2)* in boiling dimethylformamide.

(7)	R^1	R^2	R^3	Yield [%]	*t* [min]
a	CH_3	H	CH_3	30	180
b	H	$N(CH_3)_2$	CH_3	65	40
c	H	$N(CH_3)_2$	H	53	60
d	—N=CH—CH=CH—		H	76	420 [a]
e	H	T^1 [b]	H	67	30
f	H	T^2 [c]	H	46	60
g	H	T^3 [d]	H	56	90
h	H	T^4 [e]	H	68 [f]	110

[a] In boiling toluene.
[b] T^1 = 4-methyl-5-phenyl-2*H*-1,2,3-triazol-2-yl.
[c] T^2 = 4-phenyl-2*H*-1,2,3-triazol-2-yl.
[d] T^3 = 4-ethyl-5-methyl-2*H*-1,2,3-triazol-2-yl.
[e] T^4 = 2*H*-naphtho[1,2-*d*]triazol-2-yl.
[f] With 100% excess of *(2)*.

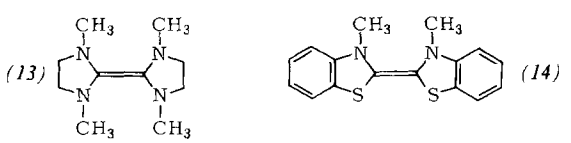
The cyclic aminals *(3)* and *(7)* can be hydrolyzed quantitatively with mineral acids to the corresponding aldehydes *(5)* and *(8)* respectively, and to the salt of *N,N'*-diphenylethylenediamine *(4)*.

Polyhydroxy compounds or their ethers containing at least one free phenolic OH group may likewise be employed in the new aldehyde synthesis, whereupon incorporation of more than one aldehyde group in the benzene nucleus is preferred. Examples are the aldehydes *(9)*–*(12)* [yields of aminal and aldehyde: *(9)*, 65 and 96%; *(10)*, 57 and 87%; *(11)*, 54 and 81%; *(12)*, 82 and 50%].



(9) *(10)* *(11)* *(12)*

Other electron-rich olefins such as *(13)*[4] (highly reactive, but difficultly accessible and highly sensitive to oxidation) and *(14)*[5] (hydrolysis of the NS-aminals difficult) have also proved to be useful reaction partners in such syntheses.



(13) *(14)*

4-(1,3-Diphenyl-2-imidazolidinyl)-2,6-dimethylphenol (3b)

A mixture of *(2)* (4.44 g, 0.01 mol) and 2,6-dimethylphenol (2.44 g, 0.02 mol) in dimethylformamide (15 ml) is heated to boiling under nitrogen for 10 min. The solvent is removed under vacuum and the residue recrystallized from isopropanol. *(3b)* is obtained as pale yellow needles in 58% yield (4.0 g, m.p. 166–167 °C).

4-Hydroxy-3,5-dimethylbenzaldehyde (5b)

A suspension of *(3b)* (2.0 g) in semi-concentrated hydrochloric acid (50 ml) is stirred for 1 h at 80 °C. The suspension is then extracted with ether and the organic phase dried over

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sodium sulphate. Subsequent removal of solvent affords 0.7 g (80%) of *(5b)* as colorless crystals (m.p. 110–111 °C).

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CAS Registry numbers:
(1a), 108-95-2; *(1b)*, 576-26-1; *(1c)*, 2078-54-8; *(1d)*, 128-39-2; *(1e)*, 87-64-9; *(1f)*, 87-65-0; *(2)*, 2179-89-7; *(3a)*, 58343-00-3; *(3b)*, 53175-56-7; *(3c)*, 53175-61-4; *(3d)*, 53175-57-8; *(3e)*, 53175-59-0; *(3f)*, 53175-58-9; *(5b)*, 2233-18-3; *(6a)*, 105-67-9; *(6b)*, 119-31-3; *(6c)*, 99-07-0; *(6d)*, 148-24-3; *(6e)*, 58343-01-4; *(6f)*, 58343-02-5; *(6g)*, 58343-03-6; *(6h)*, 40756-60-3; *(7a)*, 53247-51-1; *(7b)*, 58343-04-7; *(7c)*, 58343-05-8; *(7d)*, 58343-06-9; *(7e)*, 58343-07-0; *(7f)*, 58343-08-1; *(7g)*, 58343-09-2; *(7h)*, 58343-10-5; *(9)*, 58343-11-6; *(10)*, 28006-85-1; *(11)*, 2931-90-0; *(12)*, 58343-12-7

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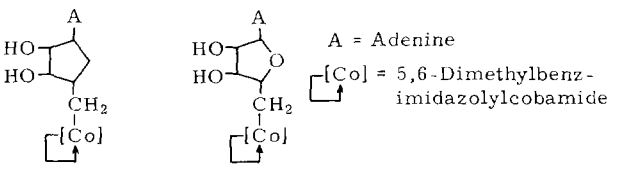
Photochemical Induction of Enzymatic Activity of a Carbocyclic Analog of Coenzyme B_{12}: A Contribution to the Elucidation of the Mechanism of Action of Coenzyme B_{12}[**]

By *G. N. Schrauzer, R. Nathan Katz, J. H. Grate*, and *T. M. Vickrey*[*]

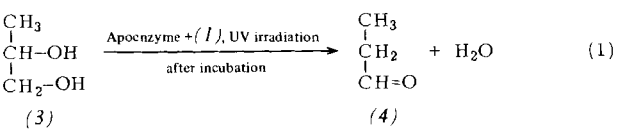
Compound *(1)*, first prepared by *Abeles et al.*[1][***], differs from coenzyme B_{12} (5'-deoxyadenosylcobalamin) *(2)* merely in that the ether-oxygen in the ribofuranosyl moiety is replaced



(1) *(2)*

by a CH_2 group. As experiments with D,L-propanediol hydrolase (dioldehydrase, E.C. 4.2.1.28) have shown, coenzyme B_{12} analog *(1)* exhibits significantly less coenzyme activity than *(2)*[1,2]. Most recent studies indicate[3] that *(1)* cannot replace the natural coenzyme *(2)*, but inhibits the action of ribonucleotide reductase from *Lactobacillus leichmannii*. Whereas the holoenzyme of dioldehydrase with *(2)* is inactivated by oxygen, the corresponding complex of *(1)* with the dioldehydrase apoenzyme has been described as air-insensitive[1]. This led us to conclude that the apoenzyme is incapable of cleaving the Co—C bond in *(1)* with similar efficiency as compared to its reaction with *(2)*.

Our own experiments with dioldehydrase from *Aerobacter aerogenes*[4] and with 1,2-propanediol *(3)* as the substrate, performed under rigorous exclusion of air and in the dark, indicate that *(1)* possesses only about 16% of the activity of the coenzyme B_{12} *(2)* under identical conditions. Brief UV irradiation[5] of the complex of apoenzyme and *(1)* after 15 min incubation produces an active enzyme which catalyzes the dehydration of 1,2-propanediol at room temperature in the dark to propionaldehyde *(4)* [Table I, and Eq. (1)].



(3) *(4)* (1)

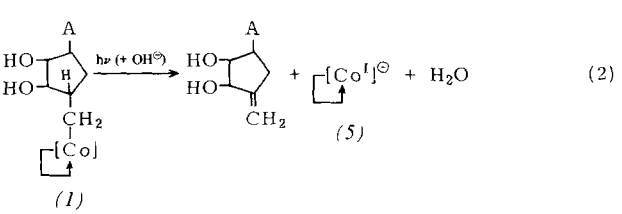
Table 1. Yields of propionaldehyde from the enzymatic dehydration of 1,2-propanediol by dioldehydrase under various conditions in the presence of *(1)* or *(2)*. Incubation time: 40 min at 23 °C.—Three ampoules of commercial apoenzyme containing 29 mg of protein each, were dissolved in 22.5 ml of deaerated 0.01 M potassium phosphate buffer (pH 8.0), the aqueous buffer solution contained 2% 1,2-propanediol and was stored under argon. All assays were performed using 0.9 ml of the enzyme solution (in closed centrifuge tubes, 15 ml capacity). The cofactors *(1)* and *(2)*, 20 nm of each, were added in aqueous form (0.1 ml). The aldehyde was determined colorimetrically as outlined in Ref. [10].

No.	System:	Yields of *(4)* [μmol]	[%]
1	Apoenzyme + *(2)*, anaerobic, normal conditions	4.60	100
2	Apoenzyme + *(1)*, anaerobic, UV-irradiated [a]	3.60	78
3	As in No. 2, but under 1 atm of N_2O	2.90	63
4	As in No. 2, under 1 atm of O_2	1.44	31
5	Apoenzyme + *(1)*, anaerobic in the dark	0.75	16
6	Denatured apoenzyme [b] + *(1)*, irradiated	0	0
7	*(1)* + 1,2-propanediol, anaerobic, irradiated	0	0
8	1,2-Propanediol + apoenzyme, irradiated	0	0

[a] The enzyme solution was irradiated for 3 min after 15 min of incubation at 23 °C.
[b] Heat-denatured enzyme.

The irradiated holoenzyme remains active for about 40—60 min; the kinetic course of the reaction closely resembles that of the enzyme with *(2)* as the cofactor under normal assay conditions. The coenzyme activity of *(1)* after irradiation becomes nearly equal to that of *(2)* at the same concentration in the dark. The irradiated enzyme complex with *(1)* is oxygen sensitive and is also partially inactivated by N_2O (Table 1). In view of the selective oxidizing action of N_2O[6], the latter observation suggests the presence of enzyme-bound vitamin B_{12s} *(5)* (*i.e.* the powerfully nucleophilic Co(I)-corrin derivative) as the actually active form of the corrinoid cofactor[7].

Vitamin B_{12s} is also formed along with vitamin B_{12r} during the anaerobic photolysis of *(1)* in weakly alkaline aqueous solutions [Eq. (2)][8]. A slow degradation to vitamin B_{12s} also occurs on interaction of *(1)* with strong bases (*e.g.* 2 N aqueous NaOH) in the dark.



(1) *(5)* (2)

The formation of vitamin B_{12s} and of olefins in the anaerobic photolysis of higher alkylcobalamins has been demonstrated previously[9]. It also has been shown that *(2)* undergoes degradation [in analogy to Eq. (2)] on interaction with bases in the dark. The base-induced formation of enzyme-bound vitamin B_{12s} is presumably responsible for the observed activity of the complex of *(1)* and the apoenzyme of the dioldehydrase; the diminished activity could be due to the higher base-resistance of *(1)* relative to *(2)*.

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[**] This work was supported by Grant GP 28485X of the National Science Foundation (USA).
[***] We thank Professor *H. P. C. Hogenkamp* for supplying us with a sample of authentic carbocyclic coenzyme B_{12} [compound *(1)*].

Our observations demonstrate that the Co—C bond of enzyme-bound *(1)* is not alternately closed and broken during the catalytic reaction with the substrate. If this were so, irradiation of the enzyme complex should not have had any significant effect on the rate of the subsequent enzymatic reaction in the dark.

The present results do not necessarily support the currently popular idea that coenzyme B_{12} dependent enzymatic reactions occur *via* organic radicals and that the coenzyme is activated enzymatically by the homolysis of the Co—C bond. On the contrary, our findings are fully consistent with the previously postulated[7, 10] heterolytic mechanism of enzymatic coenzyme B_{12}-activation[11].

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[1] *S. S. Kerwar, T. A. Smith,* and *R. H. Abeles,* J. Biol. Chem. *245*, 1169 (1970).
[2] *R. H. Abeles,* Adv. Chem. Ser. *100*, 346 (1971).
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[5] An Hg-vapor lamp manufactured by W. Gates Co. (Model 420-U 1), 360 W, was employed for the experiments.
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[8] Vitamin B_{12s} was detected unambiguously by measurements of the optical absorption spectra and subsequent alkylation with CH_3I.
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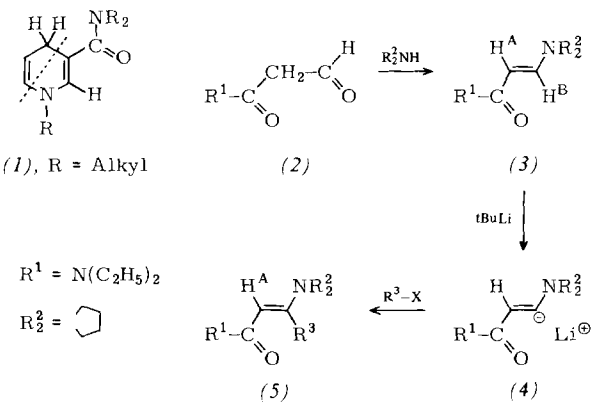
[10] *G. N. Schrauzer* and *E. A. Stadlbauer,* Bioinorg. Chem. *4*, 185 (1975).
[11] For light-induced activation of a complex of the dioldehydrase with other coenzyme B_{12} analogs, see *T. Yamane, S. Shimizu,* and *S. Fukui,* Biochim. Biophys. Acta *110*, 616 (1965).

pounds exhibiting sp^3 configuration at the aldehydic C atom. The CH acidity of sp^2 configurated C atoms is known to be greater than that of sp^3 configurated C atoms. However, this phenomenon can hardly be exploited in the case of the aldehyde itself, since addition to the carbonyl group proceeds considerably faster than dissociation of the aldehyde proton.

Having observed that 1,4-dihydronicotinamide derivatives *(1)* can be deprotonated at C-2[4] we attempted to perform nucleophilic acylations with functionally substituted aldehydes. For this purpose we converted the β-acyl aldehydes *(2)* into the enamines *(3)*; the nonparticipating carbonyl group was not protected. The first experiments with various bases showed, however, that in compounds of type *(3)* Michael addition and addition to the carbonyl group are faster than deprotonation. Nevertheless, it was also observed that the temperature dependence of these competing reactions differs. Below −100 °C deprotonation is faster so that *(3)* affords the β-acylvinyl anion *(4)*[5] almost quantitatively. Presumably, complex formation with the neighboring carbonyl group plays a role here[4]. Once formed, the anion *(4)* is stable at least up to room temperature. It can be deuterated with CH_3OD, alkylated with alkyl iodides, and acylated with esters to give polyfunctional components (Table 1)[6].



(1), R = Alkyl *(2)* *(3)* *(5)* *(4)*

Table 1. Compounds prepared [a].

Cpd.	R^3—X	^{1}H-NMR [b] H^A	H^B	H^C	B.p. [°C/torr]	Conversion [%] [c]
(3)	H—OCH_3	4.79 (d)	7.81 (d)	—	$108/2\cdot10^{-3}$	—
(5a)	D—OCH_3	4.85 (s)	—	—	≙ *(3)*	100
(5b)	CH_3^B—I	4.73 (s)	2.52 (s)	—	$90/10^{-3}$	95
(5c)	CH_3^C—CH_2^B—I	4.53 (s)	2.93 (q)	1.18 (t)	—	60
(5d)	$C_6H_5^B$—CO—OCH_3	4.97 (s)	8.18–7.20 (m)	—	150 [d]/10^{-2}	95
(5e)	*p*-CH_3^C—$C_6H_4^B$—CO—OC_2H_5	4.95 (s)	7.87–7.22 (m)	2.37 (s)	155 [d]/10^{-2}	60

[a] All compounds gave correct elemental analyses.
[b] δ values; $CDCl_3$, TMS internal standard.
[c] Conversion based on reactant. About 70–80% of the amount formed in each case was isolated.
[d] Furnace temperature on bulb tube distillation.

Nucleophilic Acylation with β-Acyl Enamines[***] [1]

By *Richard R. Schmidt* and *Jörg Talbiersky*[*]

Nucleophilic acylation with CH acidic aldehyde derivatives has acquired considerable preparative significance[1,2]. Important aldehydic intermediates appearing in this connection are 1,3-dithianes[2] and β-trimethylsilyloxy cyanides[3], *i.e.* com-

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

N,N-Diethyl-3-pyrrolidinoacrylamides (5)

To a solution of *(3)* (0.78 g, 4 mmol) in anhydrous THF (30 ml) prepared under N_2 is added at −115 °C a solution of *tert*-butyllithium (4.2 mmol) in *n*-pentane (*ca.* 1.6 M solution). After 30 min the temperature is allowed to rise to −105 °C. After another 2.5 h, the electrophile R^3—X (8 mmol) is added to the reaction mixture. The solution is warmed to room temperature and worked up with chloroform/water after 3 h. The products *(5)* were isolated by distillation (see Table 1).

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(2), 58343-35-4; *(3)*, 58343-36-5; *(5a)*, 58343-37-6; *(5b)*, 58343-38-7; *(5c)*, 58343-39-8; *(5d)*, 58343-40-1;

(5e), 58343-41-2; H—OCH_3, 67-56-1; D—OCH_3, 1455-13-6; CH_3—I, 74-88-4; CH_3CH_2—I, 75-03-6; C_6H_5CO—OCH_3, 93-58-3; *p*—$CH_3C_6H_4CO$—OC_2H_5, 94-08-6; pyrrolidine, 123-75-1

[1] β-Acylvinyl Anions, Part 1.
[2] *D. Seebach*, Angew. Chem. *81*, 690 (1969); Angew. Chem. Int. Ed. Engl. *8*, 639 (1969); Synthesis *1969*, 17.
[3] *K. Deuchert, U. Hertenstein*, and *S. Hünig*, Synthesis *1973*, 777; *S. Hünig* and *G. Wehner*, *ibid. 1975*, 180, and references cited therein.
[4] *R. R. Schmidt* and *G. Berger*, Chem. Ber., in press.
[5] For other attempts to generate β-acylvinyl anions, see *R. R. Schmidt*, Lecture at "Chemiedozententagung", Stuttgart, April 1974; *K. Kondo* and *D. Tunemoto*, Tetrahedron Lett. *1975*, 1007, 1397.
[6] In enamine systems other than *(3)*/tBuLi, account must also be taken of the deprotonations of methine groups located α relative to the enamine double bond observed by *Ahlbrecht* [7] and *Thompson* [8].
[7] *H. Ahlbrecht* and *C. Vonderheid*, Synthesis *1975*, 512, and references cited therein.
[8] *H. W. Thompson* and *B. S. Huegi*, J. Chem. Soc. Chem. Commun. *1973*, 636.

Synthesis of Trinuclear Sandwich-Like Cyclopentadienyl Complexes Containing Two Different Metal Atom Centers[**]

By *Wolfgang Kläui* and *Helmut Werner*[*]

Reaction of bis(η-cyclopentadienyl)cobalt (cobaltocene) with dialkyl phosphonates leads to trinuclear complexes of type *(1)* in almost quantitative yield:

$$3\ Co(C_5H_5)_2 + 6\ HPO(OR)_2 \longrightarrow (C_5H_5)_2Co_3[PO(OR)_2]_6 + 4\ C_5H_6 + H_2\ (?)$$

(1a), R = CH_3
(1b), R = C_2H_5

According to a crystal structure determination carried out on *(1a)*[1] the three cobalt atoms are arranged linearly. Two of them are equivalent, each being coordinated with a cyclopentadienyl ring and the phosphorus atoms of three phosphonato groups; the third (central) cobalt atom is located at a center of symmetry and is surrounded octahedrally by six oxygen atoms. *(1a)* and *(1b)* are not attacked by air and are so stable thermally that they can be sublimed undecomposed at 250 °C in a high vacuum.

During investigations on the reactivity of the trinuclear complexes *(1a)* and *(1b)* we recently found that they react with concentrated mineral acids HX and undergo protonation at the oxygen atoms. From conductivity measurements and NMR data it can be concluded that an equilibrium is established[2]:

$$(C_5H_5)_2Co_3[PO(OR)_2]_6 + 4\ HX \rightleftharpoons 2\ [C_5H_5CoPO(OR)_2\{P(OH)(OR)_2\}_2]X + CoX_2$$

(2a), R = CH_3
(2b), R = C_2H_5

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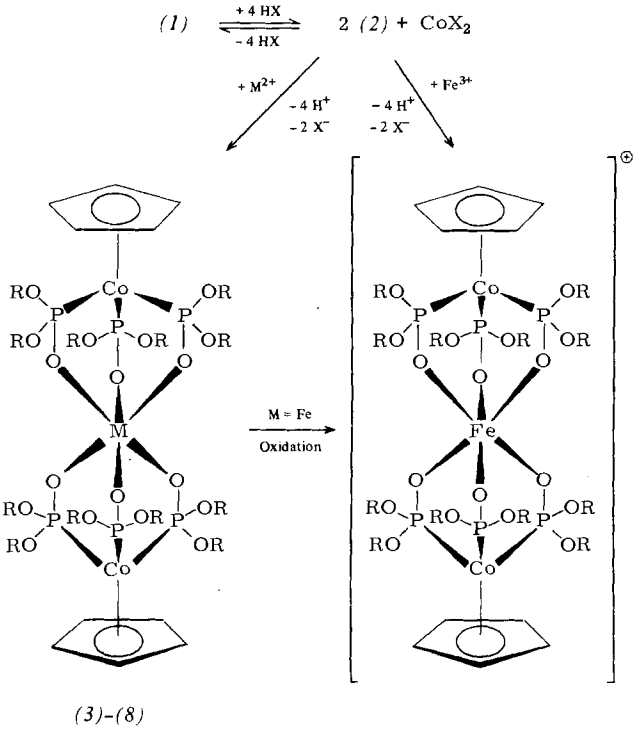
[**] This work was supported by the Schweizerischer Nationalfonds zur Unterstützung der wissenschaftlichen Forschung. We thank Herr *L. Beck* for his valuable participation in the experimental work.

We have now succeeded in performing the reverse reactions of *(2a)* and *(2b)* (X = BF_4), respectively, with Co^{2+} and synthesizing the trinuclear complexes *(1a)* and *(1b)* from the corresponding cationic monocyclopentadienylcobalt compound. Instead of compounds *(2)*, the salts $[C_5H_5Co\{PO(OR)_2\}_3BF]BF_4$[3] obtainable from them can be used as starting material. Also other transition metal ions M^{2+} react analogously to Co^{2+}; hence, trinuclear complexes of the general composition $(C_5H_5)_2Co_2M[PO(OR)_2]_6$ (*(3b)*, M = Mn; *(4b)*, M = Fe; *(5a,b)*, M = Ni; *(6a,b)*, M = Cu; *(7a,b)*, M = Zn; *(8b)*, M = Cd; R = CH_3 *(a)*, C_2H_5 *(b)*) *containing two different metals as coordination centers in the same molecule* are accessible *via* this route (see Scheme 1). A suitable solvent for the reaction is aqueous methanol, in which the salt-like starting compounds are readily soluble, whereas the neutral trinuclear complexes are very sparingly soluble. The syntheses of *(3)*–*(8)* are therefore preferably carried out as precipitation reactions.



Schema 1

As the X-ray powder diagrams of *(1b)* and *(3b)*–*(8b)* illustrate, all these compounds are isotypic and therefore probably have a similar structure to that of *(1a)*[1]. The trinuclear complexes are, with the exception of *(4b)*, light-yellow, easily crystallizable solids which are stable towards air and moderately to readily soluble in CCl_4, $CHCl_3$, and CH_2Cl_2. *(4b)* is brownish-violet; it is oxidized by air only slowly in the solid state, but rapidly in solution. Oxidation leads quantitatively to the yellow cation $[(C_5H_5)_2Co_2Fe\{PO(OC_2H_5)_2\}_6]^+$, which formally contains Fe^{3+} as central atom and can also be obtained directly by reaction of *(2b)* (X = BF_4) or $[C_5H_5Co\{PO(OC_2H_5)_2\}_3BF]BF_4$ with $FeCl_3$ (see Scheme 1). The tetrafluoroborate salt of this cation has solubility properties largely resembling those of $[C_5H_5Co\{PO(OC_2H_5)_2\}_3BF]BF_4$, *i.e.* it is readily soluble in acetone, methanol, methylene chloride, but insoluble in CCl_4 and hydrocarbons.

Like *(1)*, the trinuclear complexes *(3)*–*(6)* are also paramagnetic. The ^{1}H-NMR spectra of the diamagnetic species *(7b)* and *(8b)* are almost identical and show no influence

of the central metal atom (Zn^{2+} and Cd^{2+}, resp.) on the chemical shifts of the η-C_5H_5 and OC_2H_5 signals.

Preliminary experiments have shown that the alkaline earth metal ions Mg^{2+} and Ca^{2+} and, surprisingly, Hg^{2+} are also precipitated with the organometallic chelating agents $[C_5H_5Co\{PO(OC_2H_5)_2\}_3]^-$ (prepared from $[C_5H_5CoPO(OC_2H_5)_2\{P(OH)(OC_2H_5)_2\}_2]^+$ or $[C_5H_5Co\{PO(OC_2H_5)_2\}_3BF]^+$). Current investigations ought to clarify how selective the precipitation properties of the new chelating agents are and whether in each case (*i.e.* also with the larger M^{2+} ions) trinuclear complexes are formed in which—as in *(1a)*—the six oxygen atoms of the phosphonato groups are coordinated octahedrally to the central metal atom.

Experimental:

$[C_5H_5Co\{PO(OC_2H_5)_2\}_3BF]BF_4$ (125 mg, 0.19 mmol) is dissolved in methanol (10 ml) and the resulting solution diluted with water (10 ml). 6 ml of a 0.02 M aqueous solution of MCl_2 or MSO_4 (M = Mn, Fe, Ni, Cu, Zn, Cd) is now added slowly to the stirred solution. After 30 min the precipitate that has formed is filtered off and washed with water until no Cl^- or SO_4^{2-}, respectively, can be detected in the filtrate. The product is dried in a high vacuum, washed with methanol, re-dried, and finally recrystallized from CCl_4. Yield: 40 to 95% *(3b)–(8b)*.

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(2a), 58409-35-1; *(2b)*, 58409-37-3; *(3b)*, 58438-22-5; *(4b)*, 58438-21-4; *(5a)*, 58438-17-8; *(5b)*, 58438-23-6; *(6a)*, 58438-16-7; *(6b)*, 58438-20-3; *(7a)*, 58438-18-9; *(7b)*, 58438-24-7; *(8b)*, 58438-19-0; $[(C_5H_5)_2Co_2Fe\{PO(OC_2H_5)_2\}_6]^+$, 58409-40-8; $[C_5H_5Co\{PO(OC_2H_5)_2\}_3BF]BF_4$, 58409-39-5

[1] *V. Harder, E. Dubler*, and *H. Werner*, J. Organometal. Chem. *71*, 427 (1974).
[2] *W. Kläui, H. Neukomm, A. Salzer*, and *H. Werner*, unpublished.
[3] *G. Huttner, W. Kläui*, and *H. Werner*, unpublished.

Temperature Dependence of the Selectivity of π and σ Radicals[**]

By *Bernd Giese*[*]

A standard method for detecting[1] and assessing the reactivity[2] of short-lived intermediates consists in measuring their kinetic selectivity in an appropriate competition system. Studies on alkyl and aryl radials *(1)* have shown a mixture of $BrCCl_3$ and CCl_4 to be a suitable system[3].

$$RBr \xleftarrow[k_{Br}]{BrCCl_3} R\cdot \xrightarrow[k_{Cl}]{CCl_4} RCl$$

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

If the more reactive component $BrCCl_3$ is used in at least 10 M excess relative to the total amount of radical *(1)* then equation (a) describes the selectivity $\varkappa$.

$$\varkappa = \frac{k_{Br}}{k_{Cl}} = \frac{[RBr]\,[CCl_4]}{[RCl]\,[BrCCl_3]} \qquad (a)$$

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Little attention has hitherto been paid to the temperature dependence of the selectivity $\varkappa$ because the radicals are preferably formed from peresters or azo compounds[3] at elevated temperatures. It was only our observation that the bromides *(2)* and the chlorides *(3)* are formed instantaneously down to −20 °C[4] on reaction of organomercury salts with $NaBH_4$ in $BrCCl_3/CCl_4$ mixtures which permitted measurement of kinetic selectivity of the radicals *(1)* over a large temperature range. The reaction obeys a radical chain mechanism[5].

Initiation:
$$RHgX \xrightarrow{NaBH_4} RHgH$$
$$RHgH \longrightarrow RHg\cdot + H\cdot$$

Chain:
$$RHg\cdot \longrightarrow R\cdot + Hg$$
$$R\cdot + XCCl_3 \longrightarrow RX + \cdot CCl_3$$
(1) *(2)*, X = Br; *(3)*, X = Cl
$$\cdot CCl_3 + RHgH \longrightarrow HCCl_3 + RHg\cdot$$

Chloroform could be detected by gas chromatography; mercury was deposited directly from the solution. The selectivities of the radicals obtained from organomercury salts and from peresters[6] lie on a straight line for a given radical R· in the Eyring plot in a temperature range between −20 and +130 °C (Fig. 1).

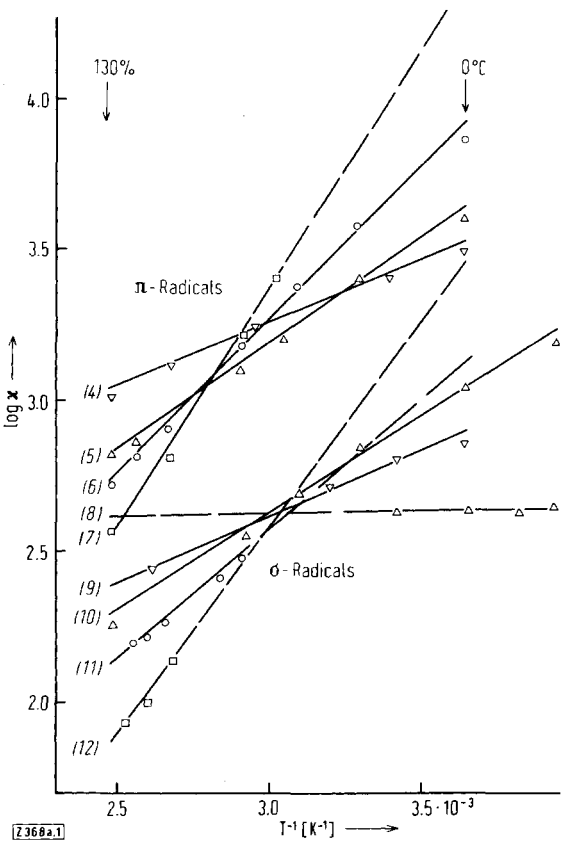


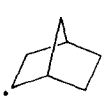
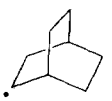
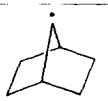
Fig. 1. Temperature dependence of the selectivity of some π and σ radicals [7] (see Table 1) in the competition system $BrCCl_3/CCl_4$. Limitations of space preclude consideration of all the radicals listed in Table 1.

Surprisingly, π and σ radicals[7] each form a pencil of straight lines in the Eyring plot, the selectivities of the π radicals coinciding in the region of 60±20 °C and those of the σ radicals at 50±10 °C (Fig. 1). Above and below these

temperatures the sequences of selectivities are reversed. At 0 °C the gradation of selectivities corresponds to expectation: thus the bulky *tert*-undecyl radical *(7)* is considerably more selective than the methyl radical *(4)*. In the series of σ radicals the shielded 2-*tert*-butylphenyl radical *(12)* is more selective than the unsubstituted vinyl radical *(8)*. At 130 °C, on the other hand, the methyl radical *(4)* is the most selective π radical and the vinyl radical *(8)* the most selective σ radical (Fig. 1).

Furthermore, above 80 °C the differences in selectivity do not decrease as expected for the π and σ radicals with rising temperature; instead they become greater. No structure-selectivity relationship exists in this competition system because the gradation of selectivity depends essentially upon the temperature.

Table 1. Differences in activation enthalpies [kcal/mol] (mean error ±5%) and in entropies of activation [e.u.] (mean error ±10%) of π and σ radicals in the competition system $BrCCl_3/CCl_4$.

π radical	$\cdot CH_3$ *(4)*	1-$\dot{C}_6H_{13}$	1-$\dot{C}_7H_{15}$	1-$\dot{C}_8H_{17}$ *(5)*	$C_4H_9C(CH_3)_2\dot{C}H_2$ [3]	2-$\dot{C}_8H_{17}$ *(6)*
$\Delta H^{\ddagger}_{Cl}-\Delta H^{\ddagger}_{Br}$	2.1	3.3	3.3	3.4	5.5	4.7
$\Delta S^{\ddagger}_{Cl}-\Delta S^{\ddagger}_{Br}$	−9.3	−5.9	−5.6	−5.3	+1.2	−0.8
π radical	c-$\dot{C}_6H_{11}$	c-$\dot{C}_7H_{13}$			$C_8H_{17}\dot{C}(CH_3)_2$ *(7)*	$CH_3\dot{C}(C_2H_5)_2$
$\Delta H^{\ddagger}_{Cl}-\Delta H^{\ddagger}_{Br}$	4.3	4.6	4.7	4.7	7.8	8.8
$\Delta S^{\ddagger}_{Cl}-\Delta S^{\ddagger}_{Br}$	−1.4	−1.2	−1.0	0.0	+8.0	+10.5
σ radical	$CH_2{=}\dot{C}H$ *(8)*	c-$\dot{C}_3H_5$ *(9)*	 *(10)*	C_6H_5 *(11)* [3]		2-t-C_4H_9—$\dot{C}_6H_4$ *(12)* [3]
$\Delta H^{\ddagger}_{Cl}-\Delta H^{\ddagger}_{Br}$	0.13	1.9	2.7	3.4		6.9
$\Delta S^{\ddagger}_{Cl}-\Delta S^{\ddagger}_{Br}$	−11.7	−6.4	−3.5	−1.5		+8.5

In contrast, the differences in activation enthalpies display a regular gradation independent of temperature (Table 1). The activation parameters are obtained from the slope and intersection of the Eyring plot according to eq. (d), which results from eqs. (b) and (c) on subtraction.

$$\log\frac{k_{Br}}{T} = \log\frac{k}{h} + \frac{\Delta S^{\ddagger}_{Br}}{2.303\,R} - \frac{\Delta H^{\ddagger}_{Br}}{2.303\,R\cdot T} \qquad (b)$$

$$\log\frac{k_{Cl}}{T} = \log\frac{k}{h} + \frac{\Delta S^{\ddagger}_{Cl}}{2.303\,R} - \frac{\Delta H^{\ddagger}_{Cl}}{2.303\,R\cdot T} \qquad (c)$$

$$\log\frac{k_{Br}}{k_{Cl}} = \frac{\Delta H^{\ddagger}_{Cl}-\Delta H^{\ddagger}_{Br}}{2.303\,R\cdot T} - \frac{\Delta S^{\ddagger}_{Cl}-\Delta S^{\ddagger}_{Br}}{2.303\,R} \qquad (d)$$

The data in Table 1 show that the differences in activation enthalpies increase with increasing shielding of the radical center in the π and σ radicals. Thus a linear correlation is obtained between the activation enthalpies and the steric E_s^c parameters[8]. Steric factors therefore dominate in these radical competition reactions. Conclusions about structurally determined properties of the intermediates are permissible only if the differences between the entropies of activation are also taken into consideration; a structure-selectivity discussion can lead to completely erroneous results[9].

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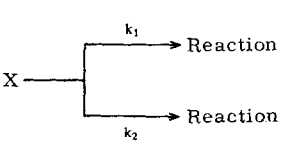
(4), 2229-07-4; *(5)*, 4606-96-6; *(6)*, 3268-43-7; *(7)*, 58281-61-1; *(8)*, 2669-89-8; *(9)*, 2417-82-5; *(10)*, 30734-19-1; *(11)*, 2396-01-2; *(12)*, 22904-45-6

[1] *R. Huisgen*, Angew. Chem. *82*, 783 (1970); Angew. Chem. Int. Ed. Engl. *9*, 751 (1970).
[2] *J. E. Leffler* and *E. Grunwald*: Rates and Equilibria of Organic Reactions. Wiley, New York 1963, p. 162.
[3] *K. Herwig, P. Lorenz*, and *C. Rüchardt*, Chem. Ber. *108*, 1421 (1975).
[4] *B. Giese, S. Gantert*, and *A. Schulz*, Tetrahedron Lett. *1974*, 3583.
[5] *C. L. Hill* and *G. M. Whitesides*, J. Am. Chem. Soc. *96*, 870 (1974).
[6] Most of the selectivities of radicals obtained from peresters are taken from ref. [3].
[7] π radicals are species bearing an unpaired electron in the p orbital. In the σ radicals investigated the single electron occupies an orbital having sp^2 character. Preliminary experiments show that sp^3 hybridized radicals (bridgehead radicals) possibly form a pencil of straight lines of their own.
[8] *T. Fujita, C. Takayama*, and *M. Nakajima*, J. Org. Chem. *38*, 1623 (1973).
[9] *B. Giese*, Angew. Chem. *88*, 161 (1976); Angew. Chem. Int. Ed. Engl. *15*, 174 (1976).

The Isoselective Relationship: Limitations and Prospects of the Structure-Selectivity Discussion[**]

By *Bernd Giese*[*]

The observation that the orders of selectivities of π and σ radicals R in the competition system $BrCCl_3/CCl_4$ are reversed between 40 and 80 °C[1] is of fundamental significance for the applicability of the principle of kinetic selectivity[2]. A condition for any structure-selectivity discussion is the existence of a linear free energy relationship[3] between the activation data of the competing reactions (1) and (2) and steric,



(1)

(2)

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

inductive, mesomeric, or any other structural parameters[4] (X = intermediate).

This condition can be formulated as the isokinetic relationship[5]:

$$\delta\Delta H_1^{\ddagger} = \beta_1 \cdot \delta\Delta S_1^{\ddagger} \quad (3)$$
$$\delta\Delta H_2^{\ddagger} = \beta_2 \cdot \delta\Delta S_2^{\ddagger} \quad (4)$$

δ indicates that only the changes in the activation data are compared on structural variation of X. The proportionality factors β_1 and β_2 are the isokinetic temperatures at which the rate constants k_1 and k_2 coincide within a given series of reactions. These isokinetic temperatures usually lie far above the range of measurement and frequently represent no more than computational quantities whose physical significance is a matter of dispute[5]. If the reactions (1) and (2) are linearly related with the same structural parameters then changes in their activation data can also be correlated with each other:

$$\delta\Delta H_2^{\ddagger} = \alpha_H \cdot \delta\Delta H_1^{\ddagger} \quad (5)$$
$$\delta\Delta S_2^{\ddagger} = \alpha_S \cdot \delta\Delta S_1^{\ddagger} \quad (6)$$

The proportionality factors α_H and α_S reflect the sensitivity of the reactions (1) and (2) towards variation of the intermediate X. Introduction of two proportionality factors allows the possibility that structural modification of X might have a varying effect on the differences between the enthalpies and the entropies of activation.

Coincidence of the selectivities k_1/k_2 is defined by eq. (7):

$$\delta \log(k_1/k_2) \equiv 0 \quad (7)$$

The temperature at which the selectivity becomes independent of variation of the intermediate X is obtained from the Eyring equation as:

$$0 \equiv \delta \log \frac{k_1}{k_2} = \frac{\delta\Delta H_2^{\ddagger} - \delta\Delta H_1^{\ddagger}}{2.303 \cdot R \cdot T_{is}} - \frac{\delta\Delta S_2^{\ddagger} - \delta\Delta S_1^{\ddagger}}{2.303 \cdot R} \quad (8)$$

$$T_{is} = \frac{(\alpha_H - 1)\delta\Delta H_1^{\ddagger}}{(\alpha_S - 1)\delta\Delta S_1^{\ddagger}} = \frac{\alpha_S(\alpha_H - 1)\delta\Delta H_2^{\ddagger}}{\alpha_H(\alpha_S - 1)\delta\Delta S_2^{\ddagger}} \quad (9)$$

This temperature T_{is}, given explicitly in eq. (9) after rearrangement of eq. (8), should be designated as the isoselective temperature. Combination of eqs. (3), (4), and (9) indicates the relation between the isoselective temperature and the isokinetic temperatures of the individual reactions.

$$T_{is} = \frac{\alpha_H - 1}{\alpha_S - 1}\beta_1 = \frac{\alpha_S(\alpha_H - 1)}{\alpha_H(\alpha_S - 1)}\beta_2 \quad (10)$$

Only when $\alpha_S = \alpha_H$, the influence of structural variation in X on the differences in the entropies and enthalpies of activation on going from reaction (1) to reaction (2) becomes equal, is the isoselective temperature T_{is} identical with the isokinetic temperatures β_1 and β_2 and therefore in most cases lies far outside the range of measurement.

$\alpha_S = \alpha_H$: $T_{is} = \beta_2 = \beta_1$

If, as in the case of reactions of carbon radicals with $BrCCl_3/CCl_4$, the change in the entropy of activation is greater than the change in enthalpy of activation[1] then the isoselective point drops to lower temperatures and can fall in the range of measurement[6].

$\alpha_S > \alpha_H$: $T_{is} < \beta_2 < \beta_1$

The proportionality factors α_S and α_H are related to the isokinetic temperatures β_1 and β_2 according to equations (3) to (6) thus:

$$\alpha_S/\alpha_H = \beta_1/\beta_2 \quad (11)$$

A difference in the isokinetic temperatures of the individual reactions ($\beta_1 > \beta_2$) accordingly reduces the isoselective temperature. Since different isokinetic temperatures are to be expected for the different reactions (1) and (2)[5] widely deviating competing reactions are of little help in the structure-selectivity discussion. Even the difference between the abstraction of bromine and chlorine by carbon radicals in the competition system $BrCCl_3/CCl_4$ leads to a reversal of the order of selectivities between 40 and 80 °C[1]. Many structure-selectivity relationships should therefore be subjected to critical scrutiny. The isoselective temperature is readily determined. By analogy with eqs. (3) and (4), eq. (12) indicates that the slope in a plot of $\Delta H_2^{\ddagger} - \Delta H_1^{\ddagger}$ *versus* $\Delta S_2^{\ddagger} - \Delta S_1^{\ddagger}$ is the isoselective temperature.

$$\delta(\Delta H_2^{\ddagger} - \Delta H_1^{\ddagger}) = T_{is} \cdot \delta(\Delta S_2^{\ddagger} - \Delta S_1^{\ddagger}) \quad (12)$$

The isoselective relationship (12) can be tested with the aid of competing radical abstraction of halogen from $BrCCl_3$ and CCl_4 for which the isoselective temperatures and the differences in the activation parameters were measured[1]. Plotting these activation enthalpies *versus* the activation entropies affords a straight line each for π and σ radicals respectively (Fig. 1). Their slopes of 320 K ± 10% and 310 K ± 5%, respectively, yield the isoselective temperature for the π radicals as 50 ± 30 °C and that for the σ radicals as 40 ± 20 °C. These values are in agreement with the temperature ranges in which the orders of selectivity of the π and σ radicals are reversed in the Eyring plot[1].

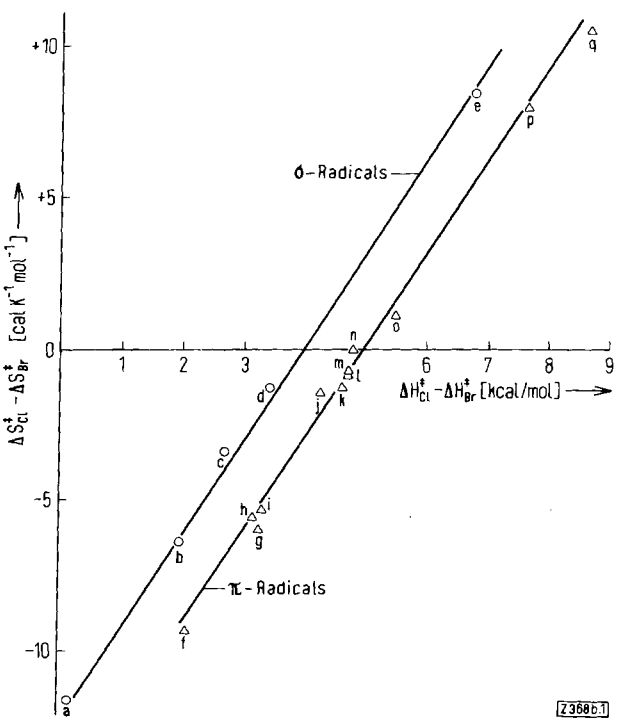

Fig. 1. Graphical check of the isoselective relation (12) for the abstraction of halogen by π and σ radicals in the competition system $BrCCl_3/CCl_4$. The activation parameters are taken from ref. [1]. The indices Br and Cl refer to the reactions of the radicals with $BrCCl_3$ and CCl_4 radicals, respectively: a, $CH_2{=}\dot{C}H$; b, c-$\dot{C}_3H_5$; c, 7-norbornyl radical; d, $\dot{C}_6H_5$; e, 2-t-C_4H_9—$\dot{C}_6H_4$; f, $\dot{C}H_3$; g, 1-$\dot{C}_6H_{13}$; h, 1-$\dot{C}_7H_{15}$; i, 1-$\dot{C}_8H_{17}$; j, c-$\dot{C}_6H_{11}$; k, c-$\dot{C}_7H_{13}$; l, 2-norbornyl radical: m, 2-$\dot{C}_8H_{17}$; n, bicyclo[2.2.2]oct-2-yl radical; o, $C_4H_9C(CH_3)_2\dot{C}H_2$; p, $C_8H_{17}\dot{C}(CH_3)_2$; q, $CH_3\dot{C}(C_2H_5)_2$.

The fact that π and σ radicals obey two different isoselective relationships (Fig. 1), leading to the appearance of two pencils of straight lines in the Eyring plot[1], opens up a further possible application: just as the isokinetic relationship is typical for a uniform reaction mechanism[5], the existence of the isoselective relationship (12) indicates formation of intermediates of the same structural type. Thus the isoselective relationship promises to become a new diagnostic criterion.

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German version: Angew. Chem. 88, 161 (1976)

CAS Registry numbers:
$CH_2=\dot{C}H$, 2669-89-8; c-$\dot{C}_3H_5$, 2417-82-5; 7-norbornyl radical, 30734-19-1; $\dot{C}_6H_5$, 2396-01-2; 2-t-C_4H_9—$\dot{C}_6H_4$, 22904-45-6; $\dot{C}H_3$, 2229-07-4; 1-$\dot{C}_6H_{13}$, 2679-29-0; 1-$\dot{C}_7H_{15}$, 3356-67-0; 1-$\dot{C}_8H_{17}$, 4606-96-6; c-$\dot{C}_6H_{11}$, 3170-58-9; c-$\dot{C}_7H_{13}$, 4566-80-7; 2-norbornyl radical, 30967-37-1; 2-$\dot{C}_8H_{17}$, 3268-43-7; bicyclo[2,2,2]oct-2-yl radical, 21246-84-4; $C_4H_9C(CH_3)_2\dot{C}H_2$, 22904-47-8; $C_8H_{17}\dot{C}(CH_3)_2$, 58281-61-1; $CH_3\dot{C}(C_2H_5)_2$, 19067-45-9

[1] *B. Giese*, Angew. Chem. *88*, 159 (1976); Angew. Chem. Int. Ed. Engl. *15*, 173 (1976).
[2] *R. Huisgen*, Angew. Chem. *82*, 783 (1970); Angew. Chem. Int. Ed. Engl. *9*, 751 (1970).
[3] *J. E. Leffler* and *E. Grunwald*: Rates and Equilibria of Organic Reactions. Wiley, New York 1963, p. 162.
[4] *N. B. Chapman* and *J. Shorter*: Advances in Linear Free Energy Relationships. Plenum Press, London 1972.
[5] *O. Exner*, Progr. Phys. Org. Chem. *10*, 411 (1973).
[6] The selectivity $\varkappa = k_1/k_2$ is defined such that reaction (2) has a higher enthalpy of activation than reaction (1); α_H is then greater than unity. It is assumed that β_1 and β_2 are positive.

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

The effects of supersonic transports on the earth's ozone mantle is the subject of a review by *H. S. Johnston*. Ozone in the stratosphere removes most of the sun's middle-ultraviolet radiation. This type of radiation has a damaging effect on DNA and causes, *inter alia*, skin cancer and bacterial mutations. Supersonic transports inject active nitrogen oxides (NO and NO_2) directly into the stratosphere. If they are not reversibly converted into nitric acid and removed as rainout after transport into the troposphere, as are the natural nitrogen oxides, they transform O_3 into O_2.—Ozone destruction by natural nitrogen oxides is counterbalanced by the photochemical regeneration of ozone. [Ground-Level Effects of Supersonic Transports in the Stratosphere. Acc. Chem. Res. *8*, 289–294 (1975); 35 references]

[Rd 824 IE—L]

Heterogeneous polymers are dealt with in an article by *E. Helfand*, with special attention being focused on interfaces between immiscible polymers and block copolymers. An attempt is made to describe qualitatively from a simple molecular point of view the entropy and energy terms which control the systems' physical features. Special consideration is given to the conditions governing phase separation. [Block Polymers, Polymer-Polymer Interfaces, and the Theory of Inhomogeneous Polymers. Acc. Chem. Res. *8*, 295–299 (1975); 28 references]

[Rd 825 IE—L]

^{13}C-NMR and the determination of the conformations of biological molecules forms the theme of an article by *I. C. P. Smith*, *H. J. Jennings*, and *R. Deslauriers*. In this sector ^{13}C-NMR spectra offer certain advantages over ^{1}H-NMR spectra. The greater dispersion of ^{13}C-NMR shifts and the removal of ^{1}H coupling by broad-band irradiation allow, *e.g.*, a detailed study of polynucleotides whose ^{1}H-NMR spectra are difficult or impossible to evaluate. Information on conformational changes of backbones can be derived from ^{13}C-^{31}P couplings.—Investigations on carbohydrates (complex glucans, polysaccharide antigens) and peptide hormones (thyrotropin-releasing hormone, oxytocin, vassopressin) are also discussed. [Carbon-13 Nuclear Magnetic Resonance and the Conformations of Biological Molecules. Acc. Chem. Res. *8*, 306–313 (1975); 45 references]

[Rd 827 IE—L]

Drugs used in the treatment of cancer are reviewed in an article by T. A. Connors. Direct chemotherapy, which is suitable for only a few forms of cancer, is being increasingly supplemented by a therapy to back up surgical measures, *i.e.* a therapy to combat metastasis at the earliest possible moment. The article is largely devoted to a description of electrophilic reactants, antibiotics, antimetabolites, and mitosis inhibitors, which are active against cancer and of attempts being made to improve their selectivity. [Drugs Used in the Treatment of Cancer. FEBS Lett. *57*, 223–233 (1975); 29 references]

[Rd 828 IE—R]

Mitochondrial ATP-phosphate exchange and the site of uncoupling of oxidative phosphorylation are reported on by *Y. Hatefi*, *W. G. Hanstein*, *Y. Galante*, and *D. L. Stiggall*. Five enzyme complexes which participate in electron transport and in oxidative phosphorylation have been isolated from bovine heart mitochondria. Four of these are the already well-known electron transfer complexes. The fifth is an energy conserving complex which catalyzes ATP-phosphate exchange and hydrolysis. The exchange reaction is sensitive toward uncoupling reagents. The photoaffinity uncoupler 2-azido-4-nitrophenol (NPA) binds only to this fifth complex, namely to a peptide of molecular weight 26000–30000. Its bonding is competitively inhibited by other uncouplers. Picrate also exhibits uncoupling action, but cannot pass through the membrane. In contrast to NPA it is a poor protonophore. [Mitochondrial ATP-P_i Exchange Complex and the Site of Uncoupling of Oxidative Phosphorylation. Fed. Proc. *34*, 1699–1706 (1975), 27 references]

[Rd 829 IE—R]

The biosynthesis of serum albumin is discussed in the light of recent knowledge by *P. N. Campbell*. It has been established that albumin, similarly to a series of other proteins, is formed from the precursor "proalbumin", which contains an additional penta- or hexapeptide on the N-terminal. This finding explains a few inconsistencies of earlier experiments on albumin biosynthesis. The additional peptide is said to be important for correct folding of the completed protein or for transport through the membrane of the endoplasmic reticulum after the synthesis. [The Biosynthesis of Serum Albumin. FEBS Lett. *54*, 119–121 (1975); 13 references]

[Rd 830 IE—R]

The antibiotic inhibition of mitochondrial ATP synthesis is the title of an article by *H. Lardy, P. Reed,* and *C.-H. C. Lin.* Fourteen antibiotics have been found which inhibit the oxidative phosphorylation and the ATPase stimulated by uncouplers in mitochondria. These antibiotics can be classified into four types according to the site of their binding to the ATPase. The first binding position binds two molecules aurovertin per molecule ATPase, the second binds efrapeptin and is probably the catalytic site. These two binding positions are found on purified ATPase. The other two binding positions occur only on membrane-bound ATPase. They are probably adjacent to each other, since several antibiotics influence both positions at the same time. [Antibiotic Inhibitors of Mitochondrial ATP Synthesis. Fed. Proc. *34*, 1707–1710 (1975); 21 references]

[Rd 831 IE—R]

Disodium tetracarbonylferrate, which can be regarded as a transition metal analog of Grignard reagents, is the subject of an article by *J. P. Collman.* The reagent *(1)* is prepared in the following manner:

$$Fe(CO)_5 + Na \xrightarrow[C_6H_5\text{-}CO\text{-}C_6H_5]{\text{Dioxane, 100 °C}} Na_2Fe(CO)_4 \cdot 1.5\ \text{Dioxane}$$

(1)

(1) can be used for transforming, *e.g.* alkyl halides and sulfonates into aldehydes, unsymmetrical ketones, carboxylic acids, esters, and amides. Conjugated olefins are reduced extremely selectively. Conversion of the ω-bromonitrile *(2)* into the

$$NC\text{-}(CH_2)_6\text{-}Br \xrightarrow[2.\ n\text{-}C_7F_{15}COCl]{1.\ (1),\ THF,\ CO} NC\text{-}(CH_2)_6\text{-}CO\text{-}C_7F_{15}$$

(2) *(3)*

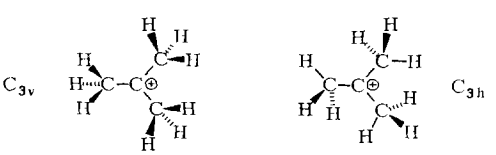
ketone *(3)* may be cited as an example; this also illustrates the failure of *(1)* to attack other functional groups. Further advantages of *(1)* are high yields and stereospecificity; its disadvantages are a pyrophoric nature and high basicity. [Disodium Tetracarbonylferrate—a Transition-Metal Analog of a Grignard Reagent. Acc. Chem. Res. *8*, 342—347 (1975); 34 references]

[Rd 832 IE—L]

The crystal face dependence of the surface chemistry of tungsten is surveyed by *R. R. Rye.* Body-centered cubic tungsten has been most thoroughly studied in this respect; the surface of its single crystals can readily be purified and characterized. Experiments conducted in ultrahigh vacuum ($<10^{-9}$ torr) revealed that the faces (111), (211), (100), and (110) differ considerably in their absorption properties. Experiments with hydrogen and ethylene are reported. [Crystallographic Dependence in the Surface Chemistry of Tungsten. Acc. Chem. Res. *8*, 347—354 (1975); 49 references]

[Rd 833 IE—L]

Theoretical approaches to the structure of carbocations is the title of a review by *W. J. Hehre.* Although hundreds of carbocations have meanwhile been generated in superacid media, the exact spatial structure of not a single species is known. For instance, does the *tert*-butyl cation *(1)* possess C_{3v} or

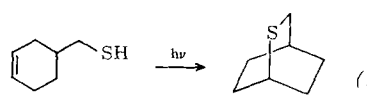


(1)

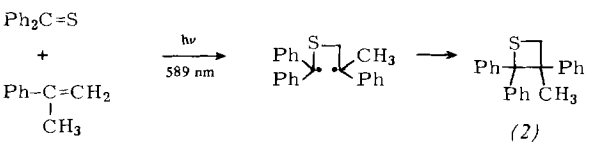
C_{3h} symmetry (propeller from)? Modern *ab initio* methods permit routine calculation of the three-dimensional structure of small organic molecules and ions. Bond lengths and angles determined by the STO-3G method deviate from the experimental values by only *ca.* 0.02 Å and *ca.* 2°, respectively, in the case of neutral hydrocarbons having up to four heavy atoms. In contrast to the predictions based on IR and Raman spectra, the STO-3G method indicates preference of the propeller form in the ground state.—Furthermore, the article also considers allyl, benzyl, and cyclopropyl cations, as well as CH_5^+ and $CH_3\text{—}CH_4^+$. [Theoretical Approaches to the Structure of Carbocations. Acc. Chem. Res. *8*, 369—376 (1975); 31 references]

[Rd 834 IE—L]

The photochemistry of organic sulfur compounds is reviewed by *J. D. Coyle.* In thiols the S—H bond is dissociated homolytically by radiation (254 nm); methanethiol decomposes into hydrogen, dimethyl sulfide, and methane. Of preparative value are, *e.g.* the addition of thiols to alkenes and the intramolecular variant of this reaction, which leads to sulfur-containing heterocycles *(1)*. In thiocarbonyl compounds, hydrogen abstraction or cycloaddition with unsaturated compounds, *e.g.* to give *(2)*, predominates.—Photoreactions of five-membered sulfur heterocycles containing 6π-electrons and of sulfonyl compounds are also discussed. [Photochemistry of Organic Sulfur Compounds. Chem. Soc. Rev. *4*, 523–532 (1975); 29 references]



(1)



(2)

[Rd 836 IE—F]

The photodegradation and stabilization of commercial polyolefins are dealt with in an article by *N. S. Allen* and *J. F. McKellar.* The term "polyolefins" covers low- and high-pressure polyethylene polypropylene, and poly(4-methyl-1-pentene). The photochemistry of the polyolefins can be divided into three main fields: photodegradation (or oxidation), sensitized photodegradation (or oxidation), and photostabilization. The photochemical properties of the polyolefins depend considerably on the state of contamination. Universally valid mechanisms cannot as yet be laid down. [Photodegradation and Stabilization of Commercial Polyolefins. Chem. Soc. Rev. *4*, 533–547 (1975); 44 references]

[Rd 837 IE—F]

Alkali-metal complexes in aqueous solution is the subject of a review by *D. Midgley.* These complexes are only weak, but nevertheless important because alkali-metal ions occur in high concentrations, *e.g.* in seawater and biological systems. Reliable data obtained by direct measurement of the equilibrium with ion-selective electrodes are now available. Inorganic and organic complexes as well as complexes with macrocyclic and biologically important compounds are discussed; in addition to stability constants the article also quotes, *inter alia,* spectroscopic and electrochemical properties. [Alkali-metal Complexes in Aqueous Solution. Chem. Soc. Rev. *4*, 549–568 (1975); 126 references]

[Rd 838 IE—F]

Chemical Applications of Pattern Recognition. By *P. C. Jurs* and *T. L. Isenhour*. John Wiley and Sons, New York—London 1975. 1st Edit., vii, 184 pp., numerous tables, bound, £ 8.25.

The reader of analytical journals will discover that increasing reference is made to publications in which operational techniques derived from information science are applied. One of these methods is *pattern recognition*. The customary application of this procedure in chemistry is for the identification of substances in a compilation of substance properties (usually spectroscopic data).

In their book *Jurs* and *Isenhour* give a survey of the principles of *pattern recognition* and how it can be applied in chemistry. As "chemical criteria" they use, *inter alia*, mass spectra, IR spectra, and also electrochemical data, the latter in some cases in combination with mass spectra, IR spectra, boiling and melting points, and so on. On a very extensive series of substances they demonstrate the results that can thus be achieved. Each chapter concludes with a literature review.

It would undoubtedly be very useful for the chemist to have an intelligible book on *pattern recognition* tailored to the chemical mode of thinking, for the analyst at least will be obliged in the foreseeable future to familiarize himself with this procedure and its possible applications. However, the authors have to a very large extent retained the language of information science, so that the book is very difficult to read, at least for chemists trained in German-language countries. However, there is also another problem that arises once again: namely, what was long a simple matter becomes unintelligible when presented in the formalism of information science!

Egon Fahr [NB 299 IE]

Instrumental Methods of Analysis. By *H. H. Willard, L. L. Merritt, Jr.*, and *J. A. Dean*. D. van Nostrand Company, New York—Wokingham 1974. 5th Edit., xix, 860 pp., numerous figs., bound, £ 8.50.

The question of the extent and method of giving chemists an insight into the "black box" of an apparatus for instrumental analysis have long been a standard discussion theme for colloquia and seminars concerned with this field. In the present book the authors provide the answers in a quite masterly manner. In 27 chapters they demonstrate, usually starting from didactically excellent drawings, the general principles and apparatus for the methods of instrumental analysis (after two chapters on electronic components: absorption spectroscopy in the UV/visible and IR regions, fluorescence spectroscopy, Raman, NMR, and ESR spectroscopy, X-ray and radiochemical methods, flame photometry, atomic absorption and emission spectroscopy, refractometry and interferometry, polarimetric, ORD, and CD methods, mass spectrometry, thermal analysis, gas chromatography, electrochemical methods, pH, ion-selective and potentiometric titrations, automated analytical procedures). The individual chapters are sensibly subdivided; they also contain proposals for instrumental investigations in practice and training exercises (problems), as well as a bibliography and details of the literature cited. The book closes with a very extensive subject index (29 pages).

The text is didactically excellent and a wealth of instructive illustrations is provided. The new and rarer techniques such as Fourier IR and NMR spectroscopy, ENDOR and ELDOR, cycloid, ion-cyclotron resonance, quadrupole and monopole mass spectrometry are also described. Unfortunately, the literature cited also contains references to journals that the German reader will hardly find useful (*e.g.* Ind. Eng. Chem., Anal. Ed.; Off. Dig. Fed. Soc. Paint Technol.).

The book is indeed one of the best in the field of instrumental analysis and is an extremely useful reference work for all who are actively teaching this profession and for those who require information, even on one brief occasion, about a specific method—the principles of its apparatus and the possibilities of its application.

Egon Fahr [NB 301 IE]

Handbook of Chemistry and Physics. Edited by *R. C. Weast*. CRC Press, Cleveland (Ohio), 1975, 56th edit., 2361 pp., bound, DM 89.—.

The fact that after 57 years of existence a book has gone through 56 editions, which differ from one another by improvements and modernizations, is probably rare even among handbooks. It indicates not only the usefulness of the book but also the commitment of the editor and the 131 scientists named as his "Collaborators and Contributors" and the "Physics Editorial Board". The word "Chemistry" ist rightly placed first in the title, for of its 2361 pages, 1497 are devoted to the three sections "The Elements and Inorganic Compounds" (421 pp.), "Organic Compounds" (797 pp.), and "General Chemical" (279 pp.). In addition to this, the book contains mathematical tables (192 pages), a Section called "General Physical Constants" (253 pages), where many points of importance and interest to the chemist are to be found, and a "Miscellaneous" chapter (352 pages) which provides much information useful in practice (densities of various solids and liquids, hardness tables, surface tensions, viscosities, critical temperatures and pressures, and a long table of "Definitions and Formulas", to mention only a few). The book is a mine of information, all of which is easily retrievable thanks to a subject index comprising 57 pages. Each table is provided with all the necessary explanations and is thus completely self-consistent. The reader is always informed what unit to assign to a numerical value, although here adherence to the international conventions would be desirable: an upper case K for kilo in KeV, or Kcal is simply wrong, cu.cm instead of cm^3 is not much better, and g-mol is today just as superfluous as g-cal. These, however, are only minor gripes. For the person who likes to have his private data bank close to his desk and who wants to find the particular value he needs with a minimum of searching, there is no handbook offering better value for money.

Helmut Grünewald [NB 305 IE]

Comprehensive Biochemistry. Vol. 29B: Comparative Biochemistry. Molecular Evolution, Part 2. Edited by *M. Florkin* and *E. H. Stotz*. Elsevier Scientific Publication Company, Amsterdam 1975. 1st Edit., xii, 284 pp., numerous figs. and tables, bound, $ 34.60.

The history of the development of various forms of life has gained a new dimension by the changeover from descriptive to quantitative biology. Moreover, refinement of the methods has made it possible to include molecular structures in the comparisons of their historical development. Microorganisms are undoubtedly the earliest inhabitants of the Earth; they have already survived at least 10^{12} generations and have thus been able to try out innumerable mutations in their efforts to utilize optimally the living space provided by the planet. Unlike algae, protozoa, and fungi, during this process they have not developed morphological variations to the same extent as their capacity for selective metabolism and biochemical mechanisms.

The first section of this volume offers a survey of the conclusions drawn about the molecular evolution of bacteria from their comparative biochemistry. In about 70 pages and with citation of nearly 250 references, *J. deLey* and *K. Kesters* give a clear description of current conclusions about the evolution of free-living into high-grade parasitic forms, the origin of mitochondria and chloroplasts, and the relationship between the deoxyribonucleic acids of various species such as can be derived from comparative analytical data. The development of catabolic and anabolic capacities, of a well-adapted energy economy, and of control mechanisms for the coordination of these processes are now clear examples of metabolic evolution, and are supplemented by comparisons of bacterial cytochromes, iron-sulfur proteins, and Gram-characteristics at the molecular level.

Using the systematic coordinates developed in volume 29A together with their complicated nomenclature, *M. Florkin* describes the biochemical evolution of animals in a comprehensive essay supported by 400 references. The essay begins with a discussion of the interactions between the environment and the biochemical individual, phylogenetic relationships are then developed from amino-acid sequences, and finally the physiological-chemical development of animals is explained with examples (some of which coincide with the author's historical exposition in volume 30). After the amino-acid constituents required for their function had been established, the protein-synthesizing machinery was adapted to the synthesis of structural proteins, enzymes, hormones, carrier proteins, and immunoglobulins; the enzymes were then again optimized for the individual cycles and these in turn were diversified in relation to the given environment. Such sweeping generalizations are never possible without serious exceptions that will cause the critical reader to reconsider specific points and, when possible, to undertake further research, thus eventually leading to new understanding.

The last chapter, also by *M. Florkin*, deals in barely 20 pages (75 references) with a mainly historical review of the ideas and experiments in the field of prebiontic development, in which appropriate space is devoted to the physicochemical models that presently seem attractive.

This volume, which brings the complete work[*] a stage nearer to its end, although more and more due to the efforts of one individual, is not only "comprehensive" but almost throughout "comprehensible". Rather than merely cataloging facts, it offers both interesting reading and a broad survey of the modern picture of molecular evolution without sidetracking into narrow specialities. The book is produced in the usual manner consistent with its price.

L. Jaenicke [NB 292 IE]

[*] Cf. Angew. Chem. *87*, 750 (1975); Angew. Chem. Int. Ed. Engl. *14*, 719 (1975).

Les Grandes Reactions de la Synthèse Organique [The Principal Reactions in Organic Synthesis]. By *J. Mathieu*, *R. Panico*, and *J. Weill-Raynal*. Hermann, Editeurs des Sciences et des Arts, Paris 1975, 1st Edit., xiv, 341 pp., bound, F. 76.—.

This book attempts to describe organic syntheses in 320 pages of text. Ionic reactions form its main part, but thermal, photochemical, and radical reactions are also well covered. There is also one chapter each on degradative and rearrangement reactions of interest to syntheses. The formula schemes are connected by a minimum of cursive text, usually only one to three lines. Each chapter begins with a short general introduction and provides an extremely concise review. Naturally the book is not exhaustive, but the authors have succeeded in providing the student with a "first library" that goes far beyond the "Organikum" and can perhaps be compared with the much larger "Weygand-Hilgetag"; still closer comparison would be with the two volumes "Formation of C—C-Chains or Aromatic Rings", also by *J. Mathieu* and *J. Weill-Raynal*. These leading industrial chemists, noted for their research work, are also University lecturers (as also is *R. Panico*), which is rare in France. Because of their experience they are well able to present current knowledge in readily understandable form. The bibliographic references are unfortunately given without the authors' names; correspondingly, there is no author index. Nevertheless, the book can be recommended as a source of information for all organic chemists interested in synthesis.

Heinz Günter Viehe [NB 293 IE]

Correlation Tables for the Structural Determination of Organic Compounds. By *M. Pestemer*. Verlag Chemie, GmbH, Weinheim 1975. 1st Edit., vi, 157 pp., bound, DM 98.—.

The book contains two pages of text (English and German), the remainder being taken up by tables. The unsaturation or ring-number R, according to which the compounds are arranged, is introduced in the text. The tables contain the molecular and structural formulas of the individual compounds, as well as the wave numbers, log ε, and the wavelengths of the measured absorption bands. About 2300 organic compounds are treated (hetero atoms N, O, S, P, and halogens).

This tabular form has the advantage of being clear and easily scanned. It would certainly have been easier for the organic chemist to handle if R had been defined more simply (*e.g.* for uncharged systems R = number of double bonds + number of rings).

As in all tabulations the choice of the compounds is arbitrary; for instance, one can find no information about phenyl azide, benzotropone, or chloronaphthalene. Some alkyl azides (pp. 24 and 41) are wrongly formulated as triazirines.

A lower price would have been welcome.

Rolf Gleiter [NB 295 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

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Exchange *in vitro* of Subunits between Enzymes from Different Organisms: Chimeras of Enzymes

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Dedicated to Professor Feodor Lynen on the occasion of his 65th birthday

Most intracellular enzymes are made up of several identical or different subunits. The more remote any two organisms are phylogenetically, the greater will be the differences in amino acid sequence of a given enzyme. Nevertheless, numerous examples exist of specific association between chemically different subunits, or even of the formation of enzyme chimeras. They span not only the boundaries between related organisms but also the deep rift between prokaryotic and eukaryotic cells. Exchange of subunits between enzymes of similar activity but differing origin can be rationalized by assuming enzymes to possess functionally defined types of three-dimensional structures.

1. Introduction

The amino acid sequence of proteins is extremely varied. Even enzymes of identical catalytic activity have far from identical amino acid compositions in different organisms. An example that has been studied particularly thoroughly is cytochrome c isolated from plants and from lower as well as higher animals; the length and amino acid sequence of the polypeptide chain has ben determined. Notwithstanding identical biological function, significant differences are found in the length of the protein chain and quite considerable variations in the sequence of amino acids. The differences are all the greater the farther the organisms under study are separated phylogenetically[1]. However, this sets no limits as to the polymorphism of enzymes, the occurrence of isoenzymes showing that even in a single organism several forms of a protein may be present having the same catalytic specificity in spite of differences in molecular structure[2].

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Under natural conditions, the amino acid sequence of a polypeptide chain also determines the biologically active three-dimensional structure: enzymes which have somehow lost their three-dimensional structure without damage to the polypeptide chain spontaneously refold, albeit at different rates, to their original shape[3]. In keeping with the enormous variety of amino acid sequences in polypeptide chains there should be just as many protein three-dimensional structures in nature.

Most intracellular enzymes contain more than one polypeptide chain[4]. One distinguishes between homopolymeric enzymes, made up of a frequently even number of identical subunits and heteropolymeric enzymes composed of different subunits. The isolated subunits are usually, but not always, inactive.

The binding between the subunits in the complete and active enzyme is mediated by highly specific interactions determined by the amino acid sequences of the subunits, for enzymes consisting of subunits also spontaneously renature to the biologically active quaternary structure after complete unfolding of the polypeptide chains[5]. The high specificity of association between the subunits of an enzyme is demonstrated by the regeneration of the original activities of all the individual enzymes on renaturation of a mixture of various dissociated

polymeric enzymes[6] Analysis of normal and of pathological hemoglobins has revealed that association to the active quaternary structure requires perfectly fitting areas of contact between the subunits. Even the slightest change, such as replacement of a single amino acid, can have an interfering effect[7].

In the light of these considerations one would hardly expect the subunits of oligomeric enzymes to combine in disregard of barriers between species to give catalytically active hybrid structures. The frequently considerable differences between the amino acid sequences of proteins serving the same function in different organisms should not permit association. Surprisingly, however, several experimental investigations have shown that such enzyme associates, named chimeras after a fabulous creature of antiquity (cf. Homer, Iliad, 6th Song, Verse 181), can nevertheless be formed *in vitro* and even *in vivo* from subunits arising from different species.

2. Hybrids of Homopolymeric Enzymes

2.1. Hybrids of Dimeric Enzymes

An example of intergeneric hybrid formation (by exchange of subunits) has long been known to occur in the case of alkaline phosphatase (EC 3.1.3.1) from bacteria. Under certain conditions, this enzyme exists as a dimer of two identical subunits. It has been isolated from both *Escherichia coli* and *Serratia marcescens*. The two proteins are chemically very different. Thus the peptide patterns obtained on tryptic degradation are not the same; and an antiserum produced by the phosphatase from *Escherichia coli* hardly reacts with the enzyme from *Serratia marcescens*.

If the two enzymes are dissociated into their subunits by treatment with 6 M urea in the presence of thioglycolic acid, the two solutions combined, and the action of the denaturing agent stopped by dilution, then a considerable proportion of the enzymatic activity is regenerated during several hours' incubation at 37 °C. Electrophoretic analysis reveals not only the bands of the original enzymes characterized by their various migration rates but protein exhibiting an electrophoretic mobility intermediate between those of the starting enzymes. We know from numerous studies on isoenzymes[2] that the appearance of proteins with modified electrophoretic mobility under these conditions is indicative of hybrid formation, *i.e.* generation of associates of subunits of the two original enzymes. *Levinthal et al.*[8] justifiably conclude that in this experiment too, in which enzymes from different species were used, a hybrid consisting of one subunit ^{e}U of the *Escherichia coli* enzyme and one subunit ^{s}U of the *Serratia marcescens* enzyme is formed according to equation (1).

$$(^{e}U)_2 + (^{s}U)_2 \rightarrow 2(^{e}U\,^{s}U) \quad (1)$$

It would seem that protein-protein interactions occur between the heterologous subunits which resemble those between the autologous subunits[8]. The hybrid protein isolated by electrophoresis displays phosphatase activity. However, this is not necessarily due to the hybrid itself, but could possibly arise from monomeric subunits or parent enzymes that may be present in a dissociative equilibrium (2)

$$2(^{e}U\,^{s}U) \rightleftharpoons 2\,^{e}U + 2\,^{s}U \rightleftharpoons (^{e}U)_2 + (^{s}U)_2 \quad (2)$$

under the conditions of activity assay. In this context, the observation that the equilibrium (2) can be shifted in either direction by foreign molecules warrants mention[9].

2.2. Hybrids of Tetrameric Enzymes

On reaction between the subunits U of tetrameric homopolymeric enzymes from two organisms a and b several hybrids can be formed. Just on the basis of their stoichiometric composition, three hybrids ($^{a}U^{b}U_3$; $^{a}U_2{}^{b}U_2$; $^{a}U_3{}^{b}U$) are possible. But for any given composition various spatial arrangements (planar or tetrahedral) are feasible in the associate. Since the equilibria between the various spatial structures may differ from those of the parent enzymes even more molecular species can occur under certain circumstances[10]. The existence of the many conceivable interspecies hybrids will be decided not only by thermodynamic aspects but also by the kinetic factors of formation and decomposition[11]. Hence the number of hybrids observed will differ from case to case.

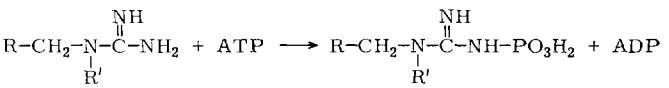
Examples of chimera formation in enzymes composed of four identical subunits have been observed for the Schiff-base-forming aldolase (EC 4.1.2.13)[12-15], L-lactate dehydrogenase (EC 1.1.1.27)[16-18], and D-glycerinaldehyde-3-phosphate dehydrogenase (EC 1.2.1.12)[11, 19-23]. Formation of interspecies hybrids in these enzymes is favored by their ready dissociation under relatively mild conditions. Accordingly, effectors which promote dissociation of the enzymes into their subunits, such as ATP in the case of D-glycerinaldehyde-3-phosphate dehydrogenase[22], greatly accelerate hybrid formation.

It is found that the phylogenetic separation between the hybridizing subunits can be very large and embraces the whole range of eukaryotes (*e.g.* beef × rabbit[13], trout × rabbit[22], Drosophila × rabbit[14], roundworm × rabbit[15, 21], yeast × rabbit[19, 20, 23]). In a number of cases the associated polypeptide chains differ so greatly from each other that they no longer show immunological cross-reactions. Evidence for hybrid formation usually follows from the difference in electrophoretic mobility between the products and the starting enzymes. Strictly speaking this merely indicates association of the subunits of different origin. Whether, and to what extent, the observed enzymatic activity is attributable to the hybrids cannot be said for the reasons stated above for the intergeneric hybrid of alkaline phosphatase (Section 2.1).

2.3. Hybrids between Enzymes of Related Activity

A particularly remarkable case of chimera formation is that between the subunits of creatine kinase (EC 2.7.3.2) from rabbit brain and L-arginine kinase (EC 2.7.3.3) of the sea cucumber. These are two enzymes which differ not only in origin but also, in spite of any similarity in the reactions catalyzed, in their substrate. They both consist of two subunits having relative molecular masses of about 40000. After dissociation of a mixture of the two enzymes into the subunits with urea, analysis of the proteins present after reactivation shows the presence of a new protein whose rate of electrophoretic migration lies between the values of the original enzymes[24]. This species is most probably the hybrid enzyme, for reaction of both creatine and arginine to form the corresponding phosphorylated products according to equation (3) is catalyzed

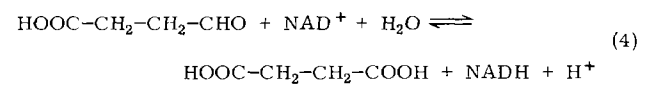
in this protein zone, whereas each of the starting enzymes can only react with one of the two substrates. However, for the same reasons as were cited for the chimeras of phosphatase the conversion of both substrates in this protein zone is not necessarily due to the hybrid itself.



(3)

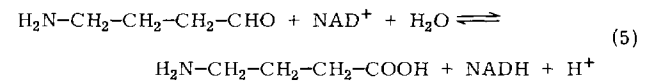
R = $COO^{\ominus}$, R' = CH_3: Creatine
R = $(CH_2)_2$-$CH(NH_2)$-$COO^{\ominus}$, R' = H: Arginine

Hybridizations between subunits of enzymes displaying different specificity even appear to occur *in vivo*. Thus apart from a dehydrogenase (EC 1.2.1.24), converting succinic



(4)

semialdehyde with the aid of NAD^+ into succinic acid according to eq. (4), and a chromatographically distinct dehydrogenase (EC 1.2.1.19), transforming 4-aminobutanal with NAD^+ into γ-aminobutyric acid according to eq. (5), two further dehydrogenases have been isolated from a *Pseudomonas*



(5)

strain which can each react with both substrates. Judging by the relative molecular masses, their composition of different subunits, and their antigenic properties, the two last-mentioned species are hybrids of the two starting enzymes[25]. Remarkably, the subunits of the two parent enzymes associate with the same stoichiometry in the hybrids in spite of the considerable difference of about 20000 in their relative molecular masses.

3. Hybrids of Heteropolymeric Enzymes

3.1. Hybrids of Enzymes with Two Different Subunits

For the reasons discussed in Section 2.1 it is very difficult to establish in the case of hybrids of homopolymeric enzymes whether the enzyme activity observed in electrophoretically isolated proteins is really attributable to the chimeras. However such proof is required to demonstrate that association of the heterologous subunits is as specific as that of the autologous subunits in the active parent enzymes. This question can be answered much more easily with hybrids of enzymes made up of different subunits (say α and β), for in such a case the isolated subunits α and β have no activity of their own, or one differing from that of the intact complex (αβ). Now if a mixture of subunit $^a\alpha$ from species a with subunit $^b\beta$ from species b displays the characteristic activity of the complete parent enzyme (αβ) it is established that the interactions between the heterologous subunits in the enzyme chimera ($^a\alpha^b\beta$) correspond to those in the parent enzymes ($^a\alpha^a\beta$) and ($^b\alpha^b\beta$), in as far as is necessary for establishment of catalytic activity.

Bacterial tryptophan synthetase (EC 4.2.1.20) consists of two subunits of different size which can readily be separated. Unlike the complete enzyme the isolated subunits, although enzymatically active, are incapable of catalyzing the reaction of indole 3-glycerophosphate with serine to give tryptophan and D-glycerinaldehyde 3-phosphate. It has been possible to combine the two subunits from a series of Enterobacteriacae *(e.g. Escherichia coli, Salmonella dysenteriae, Enterobacter aerogenes, Serratia marcescens)* over the species boundaries, in spite of considerable differences in amino acid sequence, to form hybrids exhibiting the activity of the complete parent enzymes[26–28]. In some cases it even proved possible to form hybrids from subunits of enzymes from gram negative and gram positive microorganisms[29, 30], and even of enzymes from bacteria and blue-green algae[31].

Active enzyme hybrids could also be obtained from bacterial anthranilate synthetase complex (EC 4.1.3.27) which is likewise composed of two different subunits (α and β). However, not every combination of a subunit from a bacterium a with a subunit from another bacterium b leads to an active hybrid [equations (6a) and (6b)]. If

$$^a\alpha + {}^b\beta \rightarrow (^a\alpha^b\beta) \text{ active,} \qquad (6a)$$

it does not always follow that

$$^b\alpha + {}^a\beta \rightarrow (^b\alpha^a\beta) \text{ active} \qquad (6b)$$

In these experiments subunits of enzymes from such widely differing classes of Eubacteria as *Bacillus, Pseudomonas, Acinetobacter*, and *Enterobacter* were incubated together[32–36]. That enzymatic activity does not always appear demonstrates that biological diversification can indeed also lead to modifications of the regions of the polypeptide chains of importance for interactions between the subunits.

Chimeras can even be prepared *in vitro* from bacterial protein complexes in which one subunit catalyzes the entire reaction while the other subunit merely carries the binding site of an allosteric effector; like the parent enzymes these chimeras are also subject to allosteric regulation. This is demonstrated by the formation of two active hybrids of aspartate transcarbamylase (EC 2.1.3.2) with allosteric control from the isolated subunits of *Escherichia coli* and *Salmonella typhimurium*[37].

To the above examples from the field of prokaryotes one can add the chimeras of heteropolymeric enzymes from eukaryotes. Thus the α- and β-polypeptide chains of hemoglobin from such different species as elephant, ass, mouse, and frog can associate with each other to form hybrids[38], which in all cases examined so far display the characteristic proton-dependent oxygen uptake of the complete tetramer[39].

3.2. Hybrids of Enzymes Having Several Different Subunits

3.2.1. Hybrids of DNA-Dependent RNA Polymerase

We may expect a precisely interlocking shape extending over particularly large regions, and thus very narrowly limited and specific interactions between the subunits, in those proteins which are made up of several different polypeptide chains and do not dissociate under the conditions of a biological environment.

Such an enzyme is bacterial DNA-dependent RNA polymerase (EC 2.7.7.6). It catalyzes the synthesis of RNA from ribonucleoside triphosphates under the control of DNA acting as template. The enzyme is usually isolated from bacteria as a complex of four different protein subunits α, β, β', and σ having the stoichiometric composition $\alpha_2\beta\beta'\sigma$. Only the σ subunit can sometimes be removed from the complex by ion-exchange chromatography without resorting to more drastic measures. The core enzyme having the stoichiometric composition $\alpha_2\beta\beta'$, however, is so stable that it dissociates only in detergents such as dodecyl sulfate or in 6 M urea. None of the isolated subunits displays any enzymatic activity. For this reason it cannot be established whether the function of the individual subunits in the catalytically active intact complex changes from species to species. Comparison of the RNA polymerase from *Escherichia coli* with that from various bacteriophages or from mitochondria, which contains just a single polypeptide chain[40-43], shows that DNA-dependent RNA polymerase is certainly not identical, or even similar, in all organisms. And even among bacteria, significant differences in size (Table 1) and charge are observed[44,45] between subunits from different species. Bacterial RNA polymerases are also very different in their antigenic properties. For instance, neither the enzyme from *Escherichia coli* reacts with the antibody active against the enzyme from *Micrococcus luteus*, nor does the *Micrococcus* enzyme with the antibody active against the *Coli* enzyme[45a]

Table 1. Relative molecular masses of the subunits of RNA polymerase from *Escherichia coli* and *Micrococcus luteus* [45].

Subunit	*E. coli*	*M. luteus*
Smallest subunit (α)	39000	44000
Medium-sized subunit (σ)	95000	80000
Second-largest subunit (β)	155000	146000
Largest subunit (β')	165000	151000

Nevertheless, comparison of physical data does not permit any comparison of the functions of the subunits. In such cases, functional equivalence can only be proved by mutual exchange of the subunits.

Such an exchange involving two bacteria, which differ considerably on the basis of their DNA composition and all other taxonomic criteria, *viz.* the gram-negative *Escherichia coli* and the gram-positive *Micrococcus luteus*, has been studied in detail. It proved possible to replace the subunits α, β', and σ in the RNA polymerase from *Escherichia coli* by the similar but different-sized subunits of the *Micrococcus* enzyme; DNA-dependent RNA synthesis was observed with these enzyme chimeras. Similarly, replacement of the smallest and the second-largest subunit in the *Micrococcus luteus* polymerase by subunits of the *Escherichia coli* enzyme also leads to active enzyme chimeras (Table 2)[45,46].—Attempts to obtain active hybrids containing the largest subunit from *Escherichia coli* and the second-largest from *Micrococcus luteus* have so far failed.

The resulting chimeras display differing activities, based on the amount of protein employed. It has yet to be established whether the low activity registered in some cases is attributable to an unfavorable association equilibrium between the subunits or whether the hybrid complex formed possesses a low specific activity. As in all other cases of intergeneric enzyme hybrids, precise characterization still has to be performed, especially with regard to physicochemical properties.

During the catalysis of RNA synthesis the various subunits must fulfill corresponding functions in the two bacteria. Otherwise it would be impossible to rationalize the observation

Table 2. Exchange of subunits between the RNA polymerases from *Escherichia coli* and *Micrococcus luteus* [45, 46]. +, formation of a catalytically active chimera; −, no detectable enzymatic activity.

Subunit exchanged	in *E. coli* RNA polymerase	in *M. luteus* RNA polymerase
Smallest subunit (α)	+	+
Medium-sized subunit (σ)	+	−
Second-largest subunit (β)	−	+
Largest subunit (β')	+	−

that each subunit can be replaced by a corresponding subunit from the other bacterium in at least one of the two enzymes. Moreover, any subunit can replace only one subunit in the polymerase of the other bacterium. Thus an unequivocal functional assignment of the subunits of the two bacteria is possible. At no stage of the divergent development of the two bacterial strains has a transfer of functional purposes in RNA synthesis taken place between one polymerase subunit and another.

The feasibility of exchange of subunits between various species of bacteria provides a strong indication that not only the function, but also the shape required for specific mutual association of the subunits, is very similar. Otherwise the formation of functioning enzyme chimeras would hardly be understandable. The similarity between the corresponding subunits from different bacteria is so great that mutations in the subunits can be effective beyond taxonomic boundaries. For example, a mutation in the gene of the β-subunit of RNA polymerase from *Escherichia coli* has the result that this enzyme is no longer inhibited by the antibiotic rifampicin[47]. An incorporation of the mutated subunit into the rifampicin-sensitive RNA polymerase from *Micrococcus luteus* yields an enzyme chimera that is resistant to the antibiotic[45].

Hybridization of the core complex $\alpha_2\beta\beta'$ with the subunit σ has been accomplished with such different bacteria as *Escherichia coli*, *Bacillus subtilis*, *Bacillus megatherium*, *Bacillus cereus*, *Azotobacter vinelandii*, *Pseudomonas aeruginosa*, and *Micrococcus luteus*[45,46,48-52]. Success of the experiment can be easily deduced from the appearance of enzymatic activity characteristic of the complete enzyme $\alpha_2\beta\beta'\sigma$. A protein has even been discovered in the chloroplasts of the single-cell alga *Chlamydomonas reinhardtii* which acts as the σ subunit on the core enzyme $\alpha_2\beta\beta'$ of RNA polymerase from *Escherichia coli*[53].

Reaction of the subunit σ of a bacterium a with the heterologous core enzyme of another bacterium b, does not always imply that the σ subunit of bacterium b will form an active enzyme chimera with the core enzyme of a. This observation can be utilized to test which subunit in the core enzyme $\alpha_2\beta\beta'$ is particularly important for the action of σ. Accordingly, the β' subunit is important for the function of σ in *Escherichia coli*, since σ from *Escherichia coli* can only complement the core enzyme $\alpha_2\beta\beta'$ to form the active polymerase when an RNA polymerase hybrid contains the β' subunit from *Escherichia coli*[45]. All these results support the concept of a fundamentally similar kind of organization of the RNA synthesis system in bacteria.

3.2.2. Hybrids of Bacterial Ribosomes

Similar observations as for RNA polymerase have been made on ribosomes from bacteria. Ribosomes catalyze the synthesis of proteins from activated amino acids on mRNA with participation of several "soluble" proteins. Ribosomes are made up of a larger and a smaller subunit, which are in turn made up of RNA and 34 and 20 polypeptides, respectively. It had already been observed in 1966 that the two ribosomal subunits from gram-positive *Bacillus subtilis* and gram-negative *Escherichia coli* can be cross-hybridized[54]. The functional equivalence of the subunits and the contact surfaces necessary for catalytically active interactions must therefore have been retained during the evolution of ribosome structure. The functional similarity even extends as far as the individual proteins, for it is possible to replace almost every ribosomal *Escherichia coli* protein by an equivalent protein from *Bacillus stearothermophilus*, during reconstitution of the smaller ribosomal subunit from the isolated proteins and RNA, although some of the *Bacillus stearothermophilus* proteins differ considerably from the corresponding *Escherichia coli* proteins with regard to amino acid composition, electrophoretic behavior, and immunochemical criteria[55].

Some ribosomal proteins are responsible for species-specific peculiarities as are observed, *e.g.*, in protein synthesis on the RNA of bacteriophage R 17. Such peculiarities also occur in the chimeras obtained on incorporation of these protein in heterologous ribosomes[56, 57]. Furthermore, not only can ribosomal proteins be exchanged, but also ribosomal RNA between the ribosomes of different bacteria[58].

3.2.3. Hybridizations with "Soluble" Protein Factors

Apart from ribosomes, "soluble" protein factors affecting the processes occurring at the ribosomes participate in protein synthesis. "Soluble" proteins from various bacteria were found to be active on heterologous ribosomes in spite of unmistakable immunochemical differences[59–62]. Moreover, this applies not only to the protein synthesis system from prokaryotes but also to that from eukaryotes[63, 64]. Together with the detection of chimeras of RNA polymerase and of ribosomes, all these experiments strongly suggest that the entire transcription and translation systems of prokaryotes are functionally similar in spite of differences detected between the components from different bacteria.

Joint functioning of proteins of very different origins has also been demonstrated in other complex biosynthetic systems. For instance, the acyl carrier protein in the multienzyme system of fatty acid synthesis of *Escherichia coli* can be replaced by the analogous protein from *Agrobacterium tumefaciens* or from the chloroplasts of the mesoderm of the avocado pear[65]. From among the vertebrates, the multicomponent system required for muscle contraction deserves mention. Here the Ca^{2+}-binding troponine subunit of the rabbit can be replaced by a corresponding protein from a shrimp[66].

4. Hybrids between Proteins from Prokaryotes and Eukaryotes

In Nature, a deep rift appears to exist between the prokaryotes, lacking a cell nucleus, and the eukaryotes, which do have a cell nucleus[67]. The question thus arises as to how far the protein subunits have retained their function and possibly even their ability to engage in functional cooperation across the frontier between prokaryotes and eukaryotes. Associate formation was observed between the subunits of 3-glycerinaldehyde 3-phosphate dehydrogenase from *Escherichia coli* and rabbit or pig[23]. The same has been reported for the subunits of triose phosphate isomerase (EC 5.3.1.1) from *Bacillus stearothermophilus* and chicken[23]. Initial studies on ribosomes are now also available. The ribosome subunits of eukaryotes are significantly larger than the corresponding subunits from bacteria. Nevertheless, the small ribosome subunit of the shrimp *Artemia salina*, a eukaryote, can cooperate with the large ribosome subunit from *Escherichia coli* in an albeit restricted functional interaction (*i.e.* only in the catalysis of polyuridylic-dependent dipeptide synthesis). The physicochemical interactions between subunits displaying such far-reaching phylogenetic differences are very weak. In order to detect their association glutardialdehyde was added as cross-linking agent during dipeptide synthesis; the hybrid ribosomes thus stabilized by covalent bridging could be detected by the sedimentation velocities in the ultracentrifuge[68]. In another case, cooperation of the small eukaryotic ribosome subunit from *Chlorella* with the large subunit from bacteria could be established by ribosome-dependent synthesis of guanosine tetra- and penta-phosphate[69].

Finally, it also proved possible to remove two acidic proteins from eukaryotic ribosomes of yeast and functionally replace them by two ribosomal proteins from *Escherichia coli*[70]. In this case, however, there exists an immunologically demonstrable relationship[71].

5. Conclusions

The numerous examples of chimeras of enzymes which can be formed *in vitro* can be supplemented by those arising *in vivo*, for example on crossing genetically related yeasts[72] or after fusion of somatic cells of such diverse origin as hamster, mouse, man, or rat[73]. Hybrid immunoglobulins made up of polypeptide chains arising from mouse and man have even been observed[74]. Hence, exchange of subunits between proteins from different organisms is not a special case, but rather possesses general importance throughout the whole of living Nature.

How are we to interpret the ability of subunits of widely differing origin, which vary so much in length, amino acid composition and sequence, and in their antigenic properties to mutually replace each other in oligomeric enzymes? Studies performed on hemoglobin[7] in particular have shown that precisely fitting contact surfaces are essential for cooperation of different polypeptide chains in an aggregate. Accordingly, it must be suspected that the regions necessary for mutual interactions and the function necessary for the catalyzed overall reaction are retained by subunits in oligomeric enzymes across the boundaries of species.

Preliminary evidence was provided by comparative immunochemical investigations[75]. And very strong support has come from X-ray studies: whale myoglobin and the hemoglobin of an insect larva, which differ in more than 80% of their amino acid sequence, have almost identical three-dimensional structures[76, 77]. Some confirmation may also be seen in the observation that the three-dimensional structure of

glycerinaldehyde 3-phosphate dehydrogenase consisting of four equal subunits is practically identical, whether from a bacterium or from lobster, although the two enzymes differ considerably in their amino acid sequences[78]. Other functionally related but phylogenetically different proteins likewise possess very similar structural regions[79]. The three-dimensional structure is apparently more important for function than amino acid sequence. Hence enzymes can be classified not only according to function, but also according to their three-dimensional shape.

The reason for proteins with different amino acid compositions to exhibit very similar folding may be seen in the very similar influence exerted on three-dimensional structure by many amino acids. Thus threonine, serine, or valine, leucine, and isoleucine all have a similar effect on the folding of a polypeptide chain[80]. They can thus undergo mutual replacement without causing any great change in folding. Evolutionary changes in the amino acid sequence of proteins arising from different species and yet having the same function are limited only in so far as that part of the three-dimensional structure which is essential for functioning is not allowed to alter. The existence of chimeras of enzymes thus also becomes understandable, for if the folding of polypeptide chains has changed so little in the course of evolution then the subunits of enzymes having the same catalytic activity will still fit each other spatially, regardless of barriers between species. The interlocking shape is conserved so well as to permit association, and, in many cases, catalytically active cooperation.

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Biosynthesis of the Purple Membrane of Halobacteria

By Manfred Sumper, Heribert Reitmeier, and Dieter Oesterhelt[*]

Dedicated to Professor Feodor Lynen on the occasion of his 65th birthday

Halobacteria are extremely specialized organisms. They live exclusively in saturated solutions of common salt. The cell membrane of these bacteria exhibit insular regions which can be isolated by membrane fractionation. These regions consist of a lipid matrix containing bateriorhodopsin molecules in a hexagonal crystalline arrangement. Bacteriorhodopsin is a deep purple retinal-protein complex ("purple membrane"). The purple membrane functions as a light energy converter.—How can such a differentiated membrane region arise? *In vivo* studies on the biosynthesis of the purple membrane showed another cell membrane fraction, the so-called brown membrane, to be a biosynthetic precursor. Bacterioopsin (the retinal-free protein) is initially incorporated into the brown membrane and can only form the purple membrane by crystallization in an energy-dependent reaction after prior reaction with retinal. This reaction is reversible. Removal of the retinal by formation of retinal oxime causes the purple membrane regions to disappear. Reconstitution of the bacteriorhodopsin by addition of retinal regenerates the purple membrane.

1. Introduction

During the past decade, studies on biological membrane systems have led to a generally accepted model of membrane structure known as the fluid mosaic model[1]. In essence, this model describes a membrane as a solution of oriented protein molecules in a two-dimensional lipid matrix. Such a concept allows for essentially free diffusion of both lipid molecules and membrane proteins in the plane of the membrane.

This normal case contrasts with special cases in which the membrane protein forms a two-dimensional crystalline network. Such a case is encountered in the cell membrane of halobacteria where the retinal-protein complex bacteriorhodopsin forms a crystal lattice detectable in the intact cell[2,3]. These crystalline regions can be liberated by membrane fragmentation and isolated. Owing to their intense color these membrane fragments are termed the purple membrane[4-6]. In contrast to the visual pigments (*e.g.* rhodopsin) which act as light sensors, bacteriorhodopsin functions as a light energy converter[7]. Absorption of light triggers a photochemical cycle, to which is coupled the transport of a proton through the membrane. The resulting electrochemical gradient of the proton is utilized for ATP synthesis in the cell (reviewed in ref. [8]).

The composition and structure of the purple membrane were found to be unusually simple. Knowledge of both the function and the structure makes the purple membrane a suitable model for studies on the biosynthesis of a membrane and its regulation.

2. Regulation Phenomena in the Synthesis of the Purple Membrane

2.1. Chemical Composition of the Purple Membrane

Isolated purple membrane consists of *ca.* 75% (pigment-containing) protein and 25% lipid, corresponding to about ten

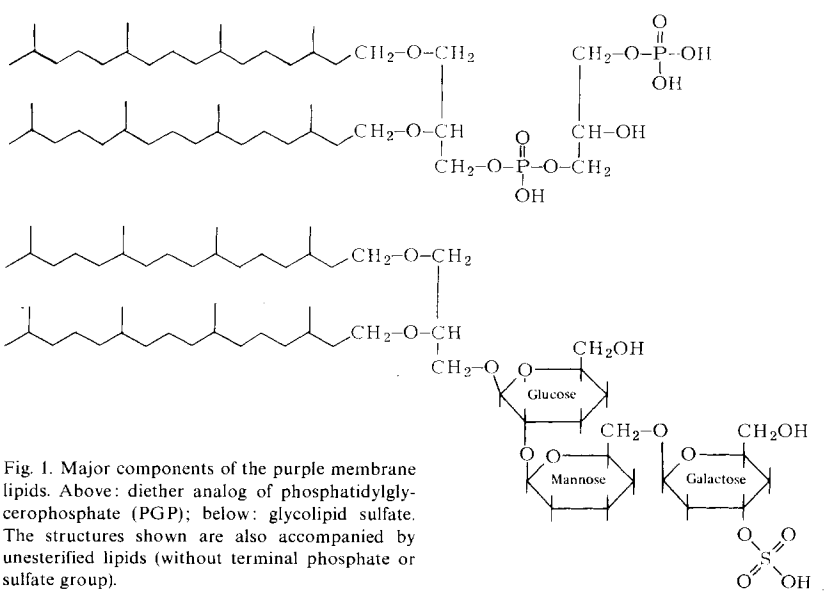

Fig. 1. Major components of the purple membrane lipids. Above: diether analog of phosphatidylglycerophosphate (PGP); below: glycolipid sulfate. The structures shown are also accompanied by unesterified lipids (without terminal phosphate or sulfate group).

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lipid molecules for every protein molecule. The sole protein species present is bacteriorhodopsin, a protein molecule having a molecular weight of about 26000 daltons and containing one retinal molecule[2]. The retinal-free protein is called bacterioopsin. More than 50% of the lipids comprise a diether analog of phosphatidylglycerophosphate, and a further 30% two glycolipids (Fig. 1). A special feature of halobacterial lipids is the absence of fatty acids; the invariable side chain of the isoprenoid alcohol dihydrophytol bound by an ether-type linkage appears in their place[9].

2.2. Influence of Oxygen and Light on Purple Membrane Synthesis

Halobacteria whose growth is not limited by restricted oxygen supply do not synthesize the purple membrane[20]. Falling oxygen partial pressure in the medium triggers the synthesis of the purple membrane, directly or indirectly. Thus, since this membrane does not belong to the constitutive equipment of the bacteria but can be utilized as a light energy converter, its function clearly appears to be that of an "emergency power generator" for the cell. When the rate of ATP synthesis *via* oxidative phosphorylation becomes inadequate the purple membrane system is brought into operation. Light does not have a similar effect on purple membrane synthesis (cf. Section 3.2).

Studies on this inducible membrane synthesis must have the ultimate aim of elucidating the time-based control of synthesis of all membrane components, *i.e.* of pigment (retinal), protein (bacterioopsin), and lipid, and in particular of answering the question of the correlation of the three synthetic pathways.

3. Synthesis of the Components of the Purple Membrane

3.1. Carotenoid Synthesis in Halobacteria

Formation of bacteriorhodopsin and thus of purple membrane is necessarily dependent on the presence of vitamin

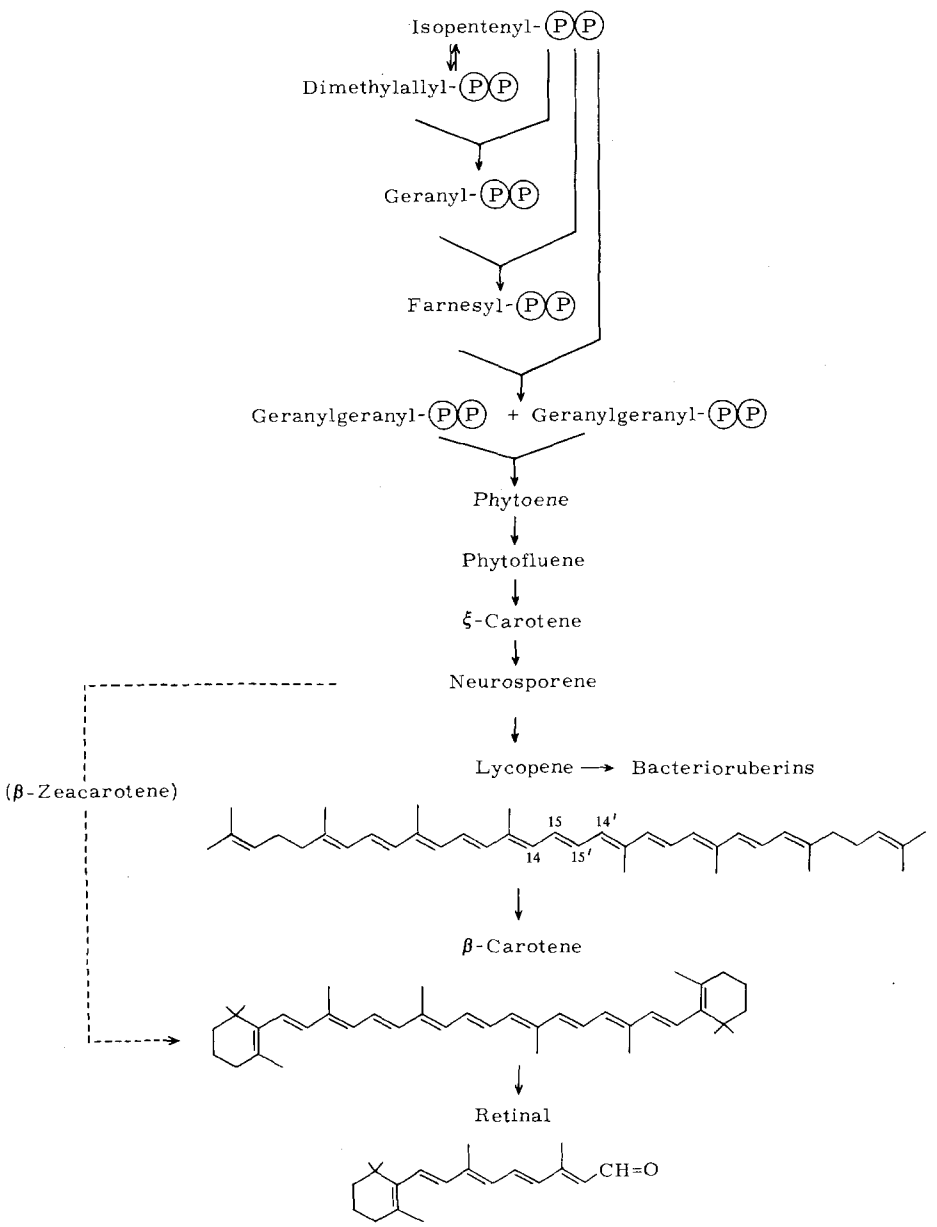

Fig. 2. Schematic representation of carotenoid biosynthesis. Ⓟ Ⓟ = pyrophosphate.

A aldehyde (retinal). In animals, retinal is formed by oxidative cleavage of the central double bond of β-carotene. β-Carotene itself is formed in plant systems from isopentenyl pyrophosphate *via* the pathway sketched out in Figure 2 and consumed by animals as provitamin A[10–15].

The two syntheses mentioned above are most probably also involved in *de novo* retinal synthesis in halobacteria, as shown by numerous recent experiments. On the one hand, the intermediates postulated in Figure 2 could be directly detected in some cases, and on the other the synthesis of β-carotene from isopentenyl pyrophosphate has recently been demonstrated in an *in vitro* system from *H. cutirubrum*[16, 17]. A special feature of carotenoid synthesis in halobacteria is the appearance of C_{50}-carotenoids, particularly bacterioruberins, as major products. They are formed by linkage of two C_5 isoprene building blocks to the ends of a C_{40}-carotenoid[18]. It remains an open question whether lycopene is a joint intermediate of β-carotene (retinal) and bacterioruberin synthesis. A conceivable alternative route is the pathway leading to β-carotene *via* β-zeacarotene as formulated in Figure 2[19].

3.2. Influence of Oxygen and Light on the Pigment Synthesis

In order to minimize interference in the analysis of biosynthetic precursors of retinal, all studies were performed with a mutant of *H. halobium* which does not synthesize bacterioruberins (*H. halobium* R_1M_1). Figure 3 compares the spectra of wild-type bacterial cells and the derived mutant cells R_1M_1. While the absorption bands of the bacterioruberins mask those of all other components in the wild-type cells, the individual absorption bands of bacteriorhodopsin, cytochromes, and lycopene can be recognized in the case of R_1M_1 cells.

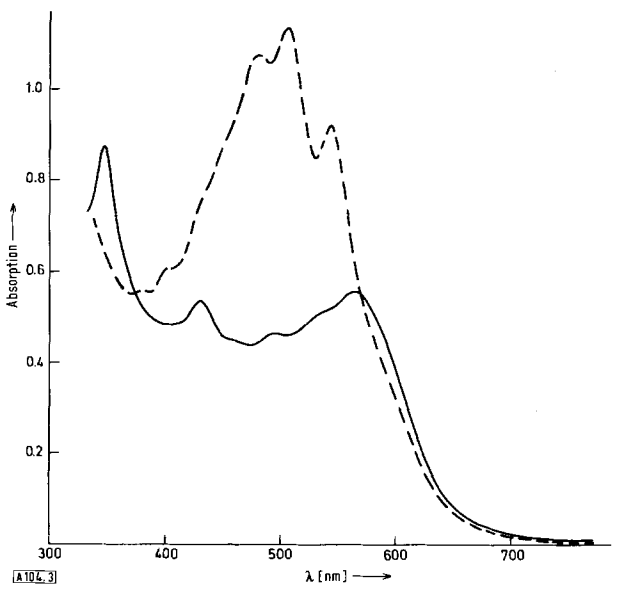

Fig. 3. Absorption spectra of halobacteria cells: wild type cells (– – – –) and R_1M_1 mutants (——).

Determination of the pigments lycopene, β-carotene, and retinal was accomplished by spectroscopy after acetone extraction of cell lyzates. The retinal bound in bacteriorhodopsin is liberated under these conditions and can therefore be determined by the specific color reaction due to *Futterman*[21].

Figure 4 shows the change of concentration of the individual pigments with time in a growing halobacteria culture. The pigment pattern for adequate oxygen supply is shown in Figure 4a, and that for insufficient aeration is seen in Figure 4b. Cells having a sufficient supply of oxygen attain only 10 to 20% of the normal retinal content. The occurrence of retinal coincides with the appearance of the purple membrane in the cells. Optimal synthesis of retinal leads to low concentrations of lycopene, and conversely a low retinal concentration results in a high lycopene level.

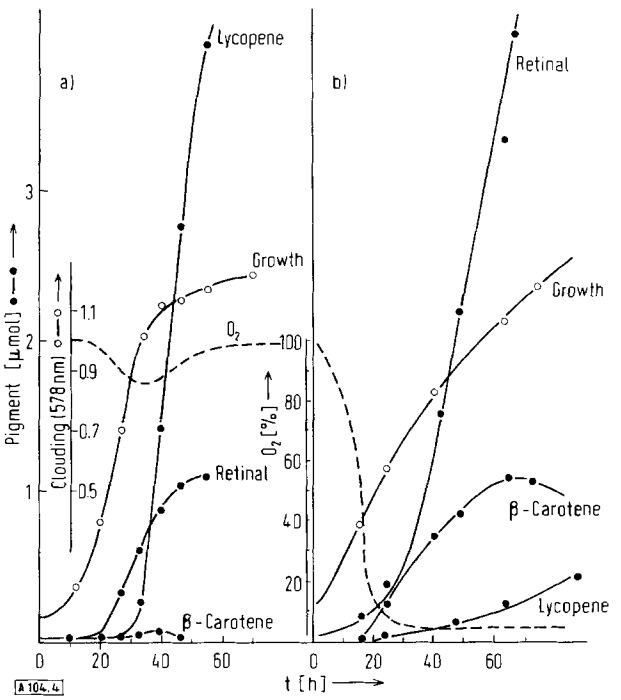

Fig. 4. Carotenoid synthesis in halobacteria under various growth conditions: a, optimal aeration; b, growth-limiting aeration.
The cells were cultured in a 14-liter Magnaferm (New Brunswick) fermenter on a complex medium (250 g NaCl, 20 g $MgSO_4 \cdot 7\,H_2O$, 2 g KCl, 3 g trisodium citrate $\cdot 2\,H_2O$, and 10 g Oxoid Pepton L 37 per liter) with illumination rpm; aeration in case b, 120 liter/h, 300 rpm.
Samples (100 ml) were taken at the times given. The pigments were extracted from the centrifuged cells with acetone/H_2O (9:1) and, after transferring to light petroleum (boiling range 50 to 70 °C), applied to an alumina column (16 g, Activity Grade II–III). Elution of β-carotene: 60 ml 20% ether in light petroleum. Elution of retinal: further 140 ml of the same mixture. Elution of lycopene: 40 ml ether. β-Carotene and lycopene were determined by spectroscopy in hexane solution, and retinal according to ref. [21]. The amounts of the pigments are given for 10 l of cell culture.

In order to examine the influence of light, the experiment depicted in Figure 4 was repeated with dark cultures. The same qualitative result was obtained; however, the β-carotene concentration is about five-fold higher. Part of the β-carotene may be destroyed on illumination; there is no compelling reason to assume intervention of a regulatory phenomenon between the synthesis of β-carotene and that of retinal.

3.3. Synthesis of Bacteriorhodopsin and of Lipids

An interesting question concerns the course of bacterioopsin synthesis with time. Conceivably, bacterioopsin could belong to the constitutive proteins of the cell; that being so it would account for a constant proportion of the protein population

of the cell in each growth phase. Figure 5 shows the protein pattern of whole cells in four consecutive growth phases and correlates it with the occurrence of the purple membrane. While almost all detectable protein species appear qualitatively unchanged the proportion of bacterioopsin increases synchronously with the appearance of the purple membrane even in the stationary growth phase of the cells.

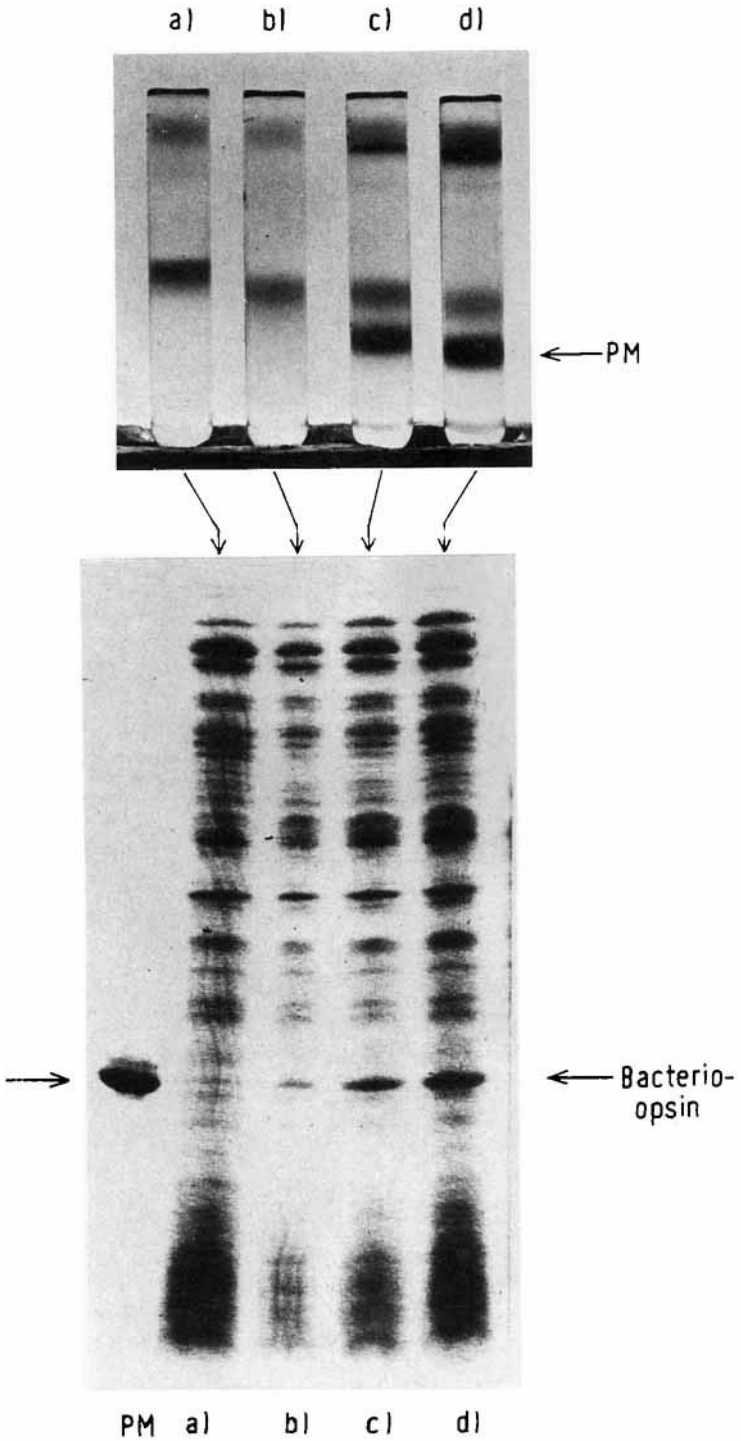

Fig. 5. Analysis of the content of purple membrane (above) and bacterioopsin (below) of halobacteria cells in four consecutive phases of the growth curve (for limiting aeration). a, logarithmic phase (47 h); b, late logarithmic phase (55 h); c and d, early (72 h) and late (101 h) stationary phase.
Equal amounts of cells were lyzed with water, placed on a sucrose density gradient (20–45%), and centrifuged at 200000 g overnight. Aliquots of the lyzate were separated by electrophoresis on polyacrylamide gels (gradient gels: 10–25%) in the presence of 0.1% sodium dodecyl sulfate. Isolated purple membrane (PM) served as bacterioopsin reference.

^{32}P and ^{35}S labeling experiments[22] were undertaken to examine the time-dependent control of synthesis of the purple membrane lipids. It was found that the purple membrane lipids are formed long before the start of retinal and bacterioopsin synthesis, *i.e.* the lipids required for formation of the purple membrane are taken from the lipid reservoir of the cell.

4. Membrane Fractions from Halobacteria

4.1. The Purple Membrane as a Differentiated Membrane Region

The isolated purple membrane contains bacteriorhodopsin molecules in a two-dimensional hexagonal crystalline arrangement[3]. Electron micrographs of intact cells obtained by the freeze fracturing technique demonstrated the same arrangement of bacteriorhodopsin in the cell membrane. Thus according to these studies, the purple membrane also exists *in vivo* as a differentiated insular region of the cell membrane[3]. The genesis of such a differentiated region is an interesting problem. Direct crystallization of bacteriorhodopsin immediately after its incorporation into the cell membrane is conceivable. Alternatively, biosynthetic precursors of the purple membrane might also exist in the form of differentiated regions in the cell membrane. Fragmentation experiments on the cell membrane and subsequent analysis of the fragments may serve to answer these questions.

Those membrane fractions which contain bacteriorhodopsin, bacterioopsin, or one of the biosynthetic precursors of retinal will be of interest in investigations on the biosynthesis of the purple membrane.

4.2. Fragmentation of the Cell Membrane

A drop in salt concentration of the medium leads to lysis of halobacteria, *i.e.* the cytoplasm of the cell is liberated[4]. Membranes are usually fractionated by density gradient centrifugation in sucrose. Density gradient centrifugation of the membrane component of halobacterial cell lyzates in the presence of 0.5 M NaCl affords a principal membrane fraction whose absorption spectrum is depicted in Figure 6. The absorption bands at 340, 419 and 560 nm are due to lycopene, cytochrome, and bacteriorhodopsin. Centrifugation of the same lyzate in the absence of NaCl gives rise to three membrane fractions A, B, C having different absorption properties. Fraction A contains all the lycopene, fraction B all the cytochrome and part of the bacteriorhodopsin, and fraction C (purple membrane) only bacteriorhodopsin. This separation suggests that the cell membrane is made up of differentiated regions.

Table 1 lists some properties of the membrane fractions A, B, and C. Owing to their characteristic colors they are known as red membrane (membrane fraction RM 340), as brown membrane, and as purple membrane.

Membrane fraction RM 340 is characterized by several unusual properties: its protein content lies below 5% of its dry weight; this is the reason for its low buoyant density. A strong absorption at 340 nm is unusual for lycopene. Addition of organic solvents (*e.g.* acetone) drastically

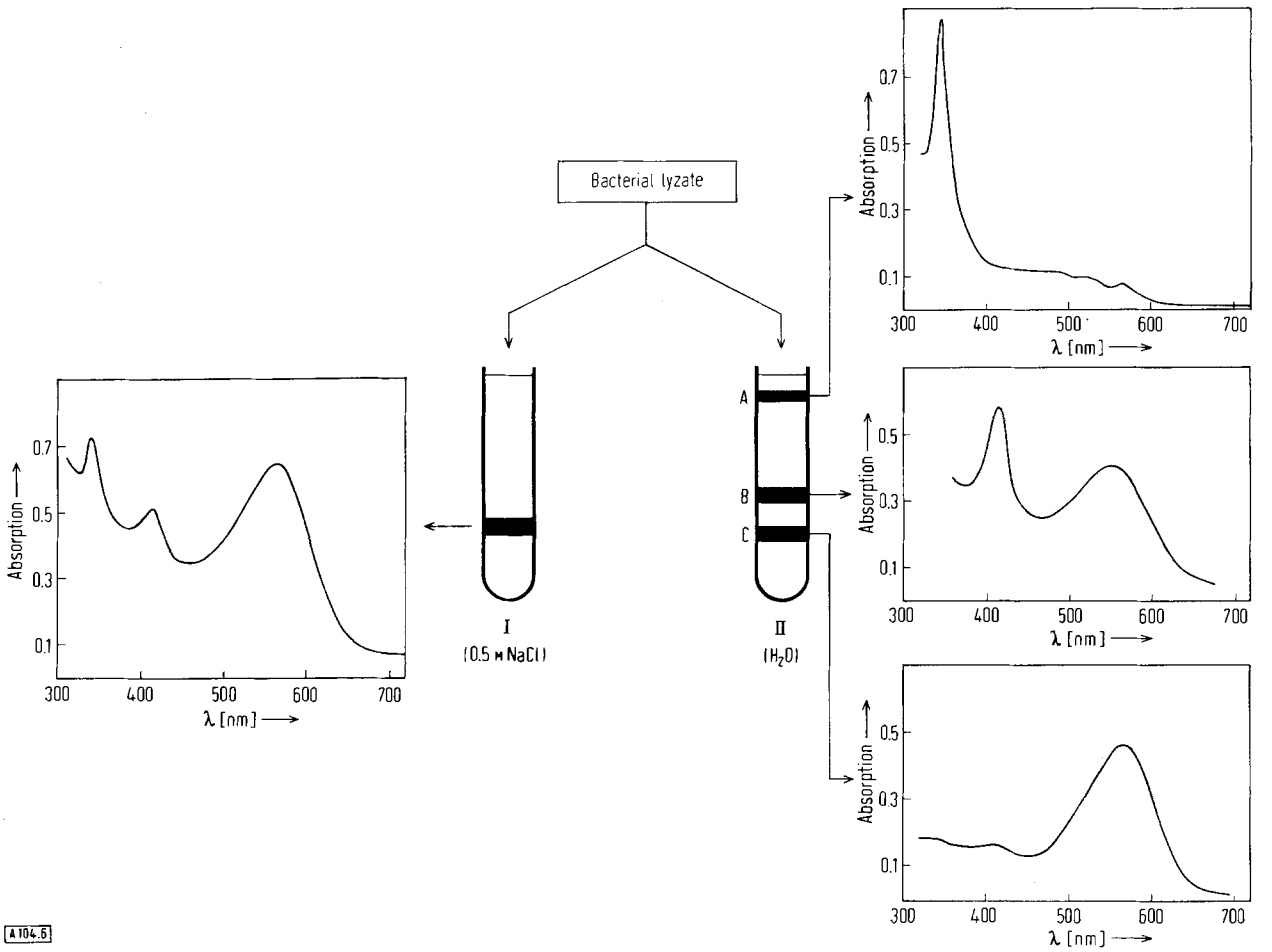

Fig. 6. Fragmentation of the cell membrane at low ionic strength. A cell lyzate was placed on a sucrose density gradient (20 to 45%) with (I) and without (II) NaCl (0.5) and centrifuged at 200000 g overnight. The spectra of the individual fractions were recorded with an Aminico DW2 instrument. A, red membrane; B, brown membrane; C, purple membrane (see text).

Table 1. Some properties of the various membrane fractions A, B, and C (see Fig. 6).

Fraction	Absorption maxima [nm]	Density [g/cm³]	Protein content [%]	Pigment
A: red membrane RM 340	340 (492, 523, 565)	*ca.* 1.06	5	lycopene
B: brown membrane	419, 560	*ca.* 1.14	?	heme, retinal
C: purple membrane	560	1.18	*ca.* 75	retinal

changes the absorption spectrum (Fig. 7); it then corresponds to that of all-*trans*-lycopene. Identity of the pigment of RM 340 and lycopene was further substantiated by its melting point and mass spectrum. The all-*trans* configuration was demonstrated by iodine-catalyzed isomerization to a mixture of the *cis* and *trans* isomers[23].

The unusual absorption behavior of lycopene in the RM 340 membrane fraction is not easy to interpret. The existence of a *cis* isomer in the membrane which transforms into all-*trans* lycopene upon addition of organic solvents appears unlikely: isomers displaying such high absorption in the "*cis* region" and so little in the visible are unknown[23]. It is more reasonable to assume that the lycopene molecule is twisted around its 14–15 and 14′–15′ single bonds (cf. Fig. 2). An *s-cis* conformer of this kind has a rod-like shape in which the π electrons of the central double bond are perpendicular to the π-electron system of the rest of the molecule. This interrupts the conjugated π-electron system containing eleven double bonds: two partial systems result, each containing five conjugated double

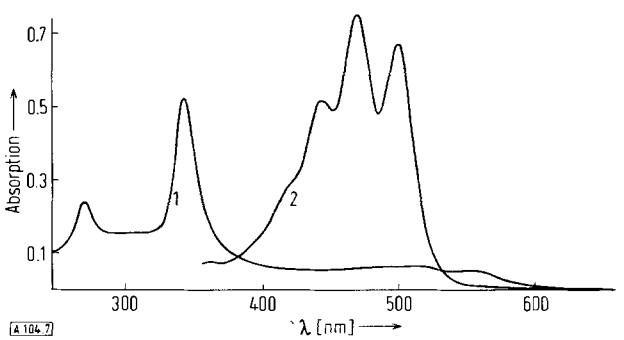

Fig. 7. Detection of lycopene as pigment of the red membrane RM 340. 1, absorption spectrum of RM 340 in water; 2, in acetone.

bonds. Thus the absorption at 340 nm and the high extinction coefficient ($\varepsilon_M = 120000\ M^{-1}\ cm^{-1}$) can be rationalized.

The brown membrane exhibits two characteristic absorptions. That at 419 nm must be assigned to a cytochrome

b type because the heme group can be extracted and as a pyridinium complex shows characteristic absorption bands at 418, 524, and 554 nm in the difference spectrum (reduced/oxidized). All the criteria tested (*e.g.* photochemical properties) indicate that the absorption band at 560 nm should be assigned to bacteriorhodopsin. The bacteriorhodopsin content of the brown membrane is also confirmed by electrophoretic analysis of the proteins present in this membrane. Two major components are obtained, one of which migrates in a manner identical to bacterioopsin and the other probably being the protein component of the heme chromophore.

5. *In vivo* Experiments on Purple Membrane Biosynthesis

All the experiments considered so far show a close correlation to exist between the synthesis of retinal and that of the purple membrane. A strategy designed to detect possible intermediates of membrane formation utilizes specific inhibitors for the synthetic pathways leading to the individual membrane component, *e.g.* inhibitors of protein biosynthesis, carotenoid synthesis, or lipid synthesis.

Table 2. Influence of nicotine on the carotenoid content of halobacteria. Halobacteria were cultured with or without nicotine in the medium. (No change in the growth rate takes place up to 1 mM nicotine.) Concerning the analysis of the pigments in the stationary phase, cf. legend of Fig. 4.

Pigment	Nicotine [mM]			
	0	0.1	0.5	1.0
Lycopene	100%	enhancement 100%–500%		
β-Carotene	100%	<1%	<1%	<1%
Retinal	100%	8%	2%	<1%

Let us now consider the results obtained so far with nicotine, an inhibitor of β-carotene formation. As shown by Table 2, formation of β-carotene in halobacteria is inhibited between 0.1 and 1 mM nicotine in the medium, with a concomitant increase in the lycopene content of the cells (nicotine cells). This result is to be expected from the known fact that nicotine inhibits cyclization of lycopene to β-carotene[24]. If the synthesis of bacterioopsin is regulated by retinal then nicotine must inhibit bacterioopsin synthesis at the same time as that of retinal. However, this is not the case. Bacterioopsin is formed in cells in the presence of nicotine (*i.e.* in the absence of retinal).

The question thus arises as to the localization of the bacterioopsin in the cell membranes of the "nicotine cells". If bacterioopsin behaves like bacteriorhodopsin, then a colorless membrane fraction of equal density and composition has to be expected in place of the purple membrane. The simplest test for bacterioopsin consists in addition of retinal, whereupon bacteriorhodopsin is reconstituted[26]. This method was applied to the membrane fractions of "nicotine cells" after density gradient centrifugation. Surprisingly, the entire bacterioopsin is found in the brown membrane (Fig. 8).

Apparently the brown membrane is a precursor of the purple membrane. Newly formed bacterioopsin occurs initially in the brown membrane and can only "crystallize to form the purple membrane" after reaction with retinal, affording bacteriorhodopsin. This working hypothesis is illustrated in Fig. 9.

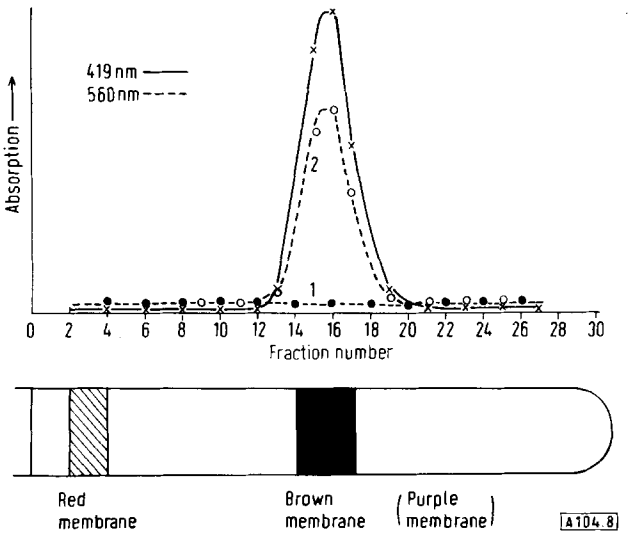

Fig. 8. Detection and localization of bacterioopsin in "retinal-free" cells. The cells were cultured in the presence of 1 mM nicotine with limiting aeration. The membrane fractions were separated by density gradient centrifugation (cf. Fig. 6). The absorption of the fractions were measured at 419 and at 560 nm before (curve 1) and after addition of retinal (curve 2).

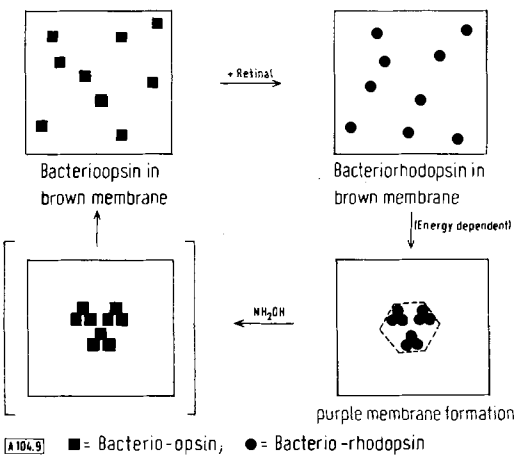

Fig. 9. Schematic representation of a working hypothesis of purple membrane formation.

Addition of retinal to "nicotine cells" should accordingly give rise to purple membrane formation, provided retinal can diffuse into the cell membrane. The feasibility of such diffusion is apparent from Figure 10. In this experiment "nicotine cells" were merely suspended in saturated salt solution (basal salt), *i.e.* without any source of energy, and treated with retinal. Once bacteriorhodopsin has formed the purple membrane should be formed by crystallization. Figure 11a shows that this does not happen, all the bacteriorhodopsin formed remaining localized in the brown membrane. Bacteriorhodopsin clearly does not crystallize spontaneously.

If the experiment of Figure 11a is repeated in the presence of a source of energy, *e.g.* L-alanine, the purple membrane is formed. The energy dependence of purple membrane formation from the brown membrane also followed from the ability of light to serve as energy source for this process in place of alanine. Since light absorbed by bacteriorhodopsin raises

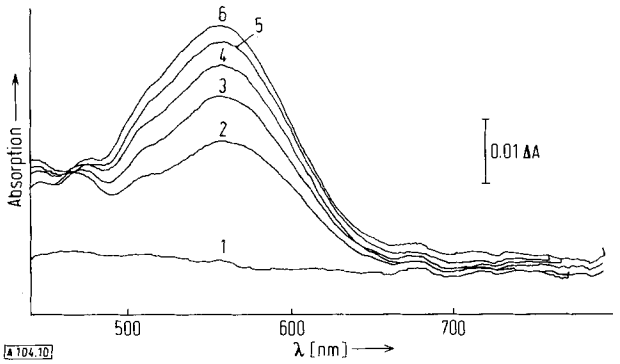

Fig. 10. Reconstitution of bacteriorhodopsin in "retinal-free" cells by addition of retinal.
Cells cultured in the presence of nicotine (1 mM) were resuspended in basal salt containing 1 mM nicotine (250 g NaCl, 2 g KCl, 20 g $MgSO_4 \cdot 7H_2O$ per liter). After treatment of the cell suspension with retinal the difference spectrum was recorded (Aminco DW 2) at various times: 1, before addition of retinal; 2–6, after 11, 18, 31, 77, and 122 min.

the ATP level of the cells it seems an obvious step to assume the occurrence of some ATP-dependent modification of one of the purple membrane components.

on abstraction of retinal from the purple membrane by reaction with hydroxylamine (cf. Fig. 9). X-Ray diffraction experiments indicate that the purple membrane loses its lattice structure on bleaching with NH_2OH and regains it on addition of retinal[25]. Isolated patches of purple membrane necessarily constrain the bacterioopsin to adopt a dense packing so that no change in density is to be expected for the bleached purple membrane (apomembrane); nor has any such change been detected experimentally. In contrast, a lateral diffusion of bacterioopsin in the cell membrane should be feasible in intact cells leading to dissolution of the purple membrane regions (cf. Fig. 9). Confirmation is provided by density gradient centrifugation of the lyzates obtained from cells treated with NH_2OH and analysis of the membrane fractions: the entire bacterioopsin is now located in the brown membrane.

6. Conclusion

The studies described in this article merely represent the first steps toward an understanding of the synthesis and association of membrane building blocks and the regulation of

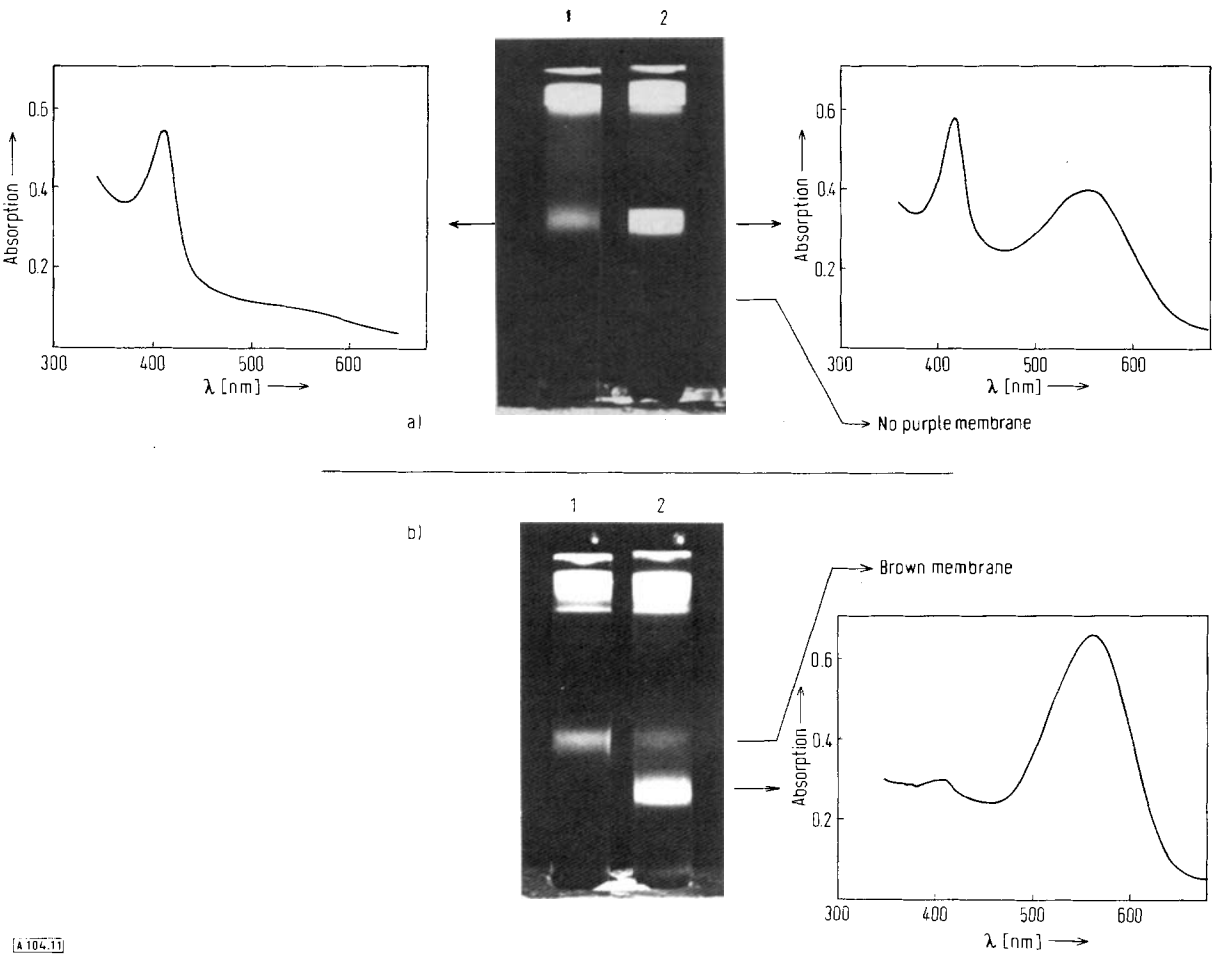

Fig. 11. "Crystallization" of bacteriorhodopsin in the brown membrane to from the purple membrane. a) "retinal-free" cells were suspended in basal salt (containing 1 mM nicotine); one half was treated with retinal and incubated at 40°C for 8 h. (For analysis of the membrane fractions see Fig. 6.) 1, without retinal; 2, with retinal. b) as for a) except for addition of 0.5% L-alanine to the incubation medium. 1, without retinal; 2, with retinal.

As shown by the above experiments, bacterioopsin is not able to form the lattice structure of the purple membrane. Such a property of bacterioopsin should also be detectable such processes. However, they have already clearly demonstrated the suitability of the halobacterial system for experimental work in this area.

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Neuron Models

By Bernd Hamprecht[*]

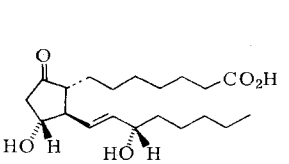
Dedicated to Professor Feodor Lynen on the occasion of his 65th birthday

The nervous system is made up of several kinds of cells which should ideally be examined separately in biochemical studies. Since we are not yet able to isolate the different kinds of cells, use is made of cell lines derived from a single cell which are isolated from tumors of the nervous system and which can be reproduced at will in the same way as bacteria. They include cell lines isolated from a mouse neuroblastoma which exhibit some of the properties of nerve cells. Hybrid cells obtained by fusion of mouse neuroblastoma cells with rat glioma cells display even more characteristics of nerve cells. This article considers properties which justify our regarding the hybrid cells as neuron models. Application of the cells to problems of the nervous system is then demonstrated: 1) processing of information arriving in the form of mutually opposing hormonal signals; 2) mode of action of morphine.

1. Introduction

The brain is a complex structure consisting of various cell types. If the cells of the blood vessel system are left out of account, the most important cells are the neurons (nerve cells) and the glial cells; each type comprises about 50% of the cell mass in the brain.

The neurons are joined together by connections called synapses and possess a highly specialized and characteristic structure that can be seen in an electron microscope (Fig. 1). At the synapses information is transferred from one (presynaptic) nerve cell to another (postsynaptic) nerve cell. The membranes of the presynaptic and the postsynaptic cells are separated by a gap. Information is transferred by means of a small molecule (the neurotransmitter) which passes from the presynaptic cell into the synaptic gap when the presynaptic cell is excited. The neurotransmitter diffuses from the presynaptic membrane through the synaptic gap onto the membrane of the postsynaptic target cell. There it becomes bound to highly specific receptors and in that process discharges electric signals into the target cell or suppresses signals that have been evoked by other neurotransmitters in other synapses



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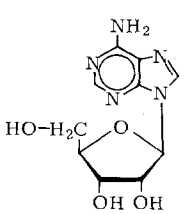

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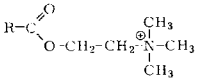
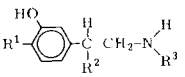
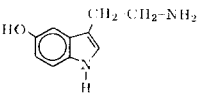
Table 1. Neurotransmitters and neurotransmitter candidates (NT) as well as some analogs (An).



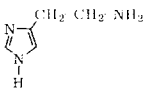
(1a), R = CH_3, acetylcholine (NT)
(1b), R = NH_2, carbamoylcholine (An)



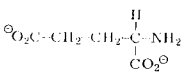
(2a), R^1 = OH, R^2 = R^3 = H, dopamine (NT)
(2b), R^1 = R^2 = OH, R^3 = H, norepinephrine (NT)
(2c), R^1 = R^2 = OH, R^3 = $CH(CH_3)_2$, isoproterenol (An)
(2d), R^1 = H, R^2 = OH, R^3 = CH_3, phenylephrine (An)



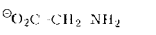
(3), serotonin (NT)



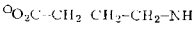
(4), histamine (NT)



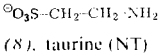
(5), glutamate (NT)



(6), glycine (NT)



(7), γ-aminobutyrate (NT)



(8), taurine (NT)

(9), substance P (NT)

on the same cell. Not only the experimentally demonstrated and the potential neurotransmitters [acetylcholine *(1a)*, dopamine *(2a)*, norepinephrine *(2b)*, serotonin *(3)*, histamine *(4)*, glutamate *(5)*, glycine *(6)*, γ-aminobutyrate *(7)*, taurine *(8)*, the undecapeptide "substance P" *(9)*; see Table 1] but also substances that probably act as modulators of neuronal activity [prostaglandins such as prostaglandin E_1 *(10)* and adenosine *(11)*] have been recognized; all these substances are known collectively as neurohormones.

According to the morphology, one differentiates five types in the cerebellar cortex; they are arranged in space in an extremely precise and constant manner and are connected with one another by means of synapses[1]. The neurons can be divided into classes from many different points of view. One possibility is to arrange them according to the type of neurotransmitter that they synthesize and use for the transfer of information, *i. e.* according to their output; thus, one speaks of cholinergic, dopaminergic, adrenergic, and other neurons. They could also be arranged according to the neurotransmitters and neurohormones to which they respond, *i. e.* according to their input. There are probably 20 or more neurotransmitters, neurotransmitter "candidates", and other hormone-like factors[2]. Different combinations of receptors for these substances on the neuron surface could lead to a very large number of different cell types. It is not known whether there

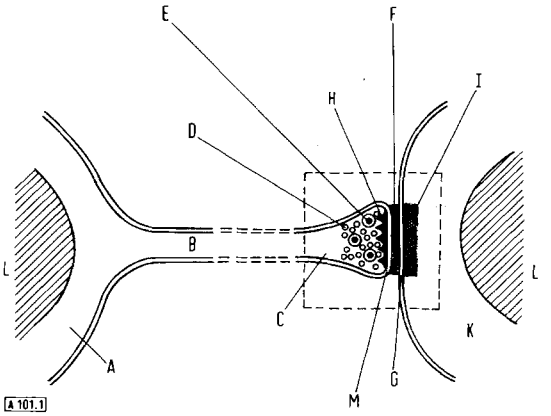


Fig. 1. Diagrammatic sketch of a synapse between two nerve cells. The left-hand, presynaptic nerve cell (A) sends out a cell extension (B) (called a nerve fiber or axon), whose end is thickened to a flask-like shape (C). The nerve ending contains, *inter alia*, a large number of small vesicles which store a neurotransmitter. When the neurotransmitter is acetylcholine the vesicles have a diameter of 500 Å, when it is norepinephrine a diameter of 2000 Å. Because of the electron-transparency of the samples prepared for electron microscopy, the small vesicles storing acetylcholine are called "clear" vesicles (D); correspondingly, the large vesicles storing norepinephrine are called "dense-core" vesicles (E) because of their dark nucleus. The nerve ending is separated from the postsynaptic membrane (G) by the synaptic gap (F) 250 Å wide. The synaptic gap contains proteins which fasten the presynaptic and postsynaptic cells very firmly to one another. In the electron microscope presynaptic and postsynaptic specializations (H and I) are also seen, their functions being, however, unknown. The extent of the synapse is the square marked by a broken line. It should be noted that the relative sizes in the sketch do not correspond to reality: the nerve ending is drawn too large in relation to the two cells, the vesicles too large in relation to the nerve ending, and the gap too large in relation to the vesicles.—K = postsynaptic cell, L = cell nucleus, M = presynaptic membrane.

is a lowest and a highest value for the number of neurohormones to which a single nerve cell reacts, *i. e.* to the number of neurohormones for which the cell can possess receptors on its surface.

Glial cells are divided essentially into two classes, astrocytes and oligodendrocytes. The latter surround the nerve fibers (axons) extending from the neurons in the same way as cable insulation surrounds a cable. Little, however, is known about the function of astrocytes.

The biochemistry of the nervous system can be investigated on tissue sections or tissue homogenates. This, however, only yields mean values averaged for all the cells and it must be taken into consideration that external influences can trigger off chains of interactions between different cells and that constituents previously divided among different cells can occur in one compartment in the homogenate. The observed effects can thus be ascribed to one definite cell type only with difficulty; just as the chemist likes to work with pure substances, so the biochemist wants pure enzymes and "pure cells"; he would like to study each type of cell in isolation and then reconstruct the original complex structures gradually by combination of the various cell types or to create them anew for study. In such investigations methods from the disciplines of biochemistry, cell biology, pharmacology, electrophysiology, and immunology will all prove helpful.

Fractions of cut-off nerve endings, so-called synaptosomes, can be centrifuged off from brain homogenates[3]; after further fractionation, these are particularly well suited for many biochemical investigations.

To learn the properties of individual cell types one can "dissociate" brains into individual cells by enzymes and mechanical forces and separate these cells by centrifuging[4, 5].

The low viability and purity of the enriched neuron or glial-cell fractions limits their use and the information obtainable from the experimental results.

Dissociated brain or spinal cord cells attach themselves from suspensions to the bottom of a Petri dish[6]. Some of the cells then reproduce themselves. By choosing the conditions of the cell culture one can decide whether mainly neurons or mainly glial cells shall survive, but presumably such cultures are also mixtures of various cell types. In mixed cell cultures from nerve and muscle tissues it has proved possible to establish synapses between the neurons and the muscle cells[7-12].

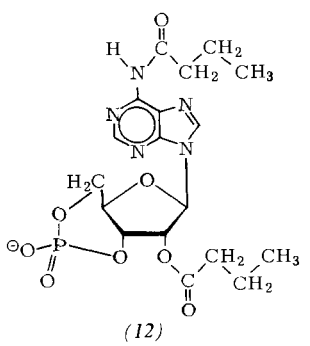
If suspensions of dissociated embryonal brain cells are shaken in small Erlenmeyer flasks for a few days at a specific rate, they reaggregate into structures resembling the original tissue[13-17]. In this process functions of the nervous system are produced that were absent in the embryonal cells[15,17].

2. Neuroblastoma Cells

Another way of obtaining "pure cells" is by isolation and cloning (*i.e.* reproduction of the descendants of a single cell) of cells from tumors of the nervous system. These cells can be cultured like microorganisms in large quantities. They are generally grown as a coating on the bottom of a plastic culture vessel incompletely filled with a culture medium. *Gabriella Augusti-Tocco*, in *Gordon Sato*'s laboratory, was the first to succeed in adapting neuroblastoma cells to culture conditions and to demonstrate that they possessed the differentiated functions of the nervous system[18]. The neuroblastoma was a spontaneous tumor found in a newborn mouse in the neighborhood of the spinal column; it has been further cultured for more than 30 years as a transplantation tumor. Several laboratories have confirmed these experiments and extended them further[19-22]. Currently studies are also in progress with neuroblastoma cells from man[23] and rats[24]. Since the properties of neuroblastoma cells have been summarized in several reviews[6,11,25-27], the present article will be restricted to mentioning only some of their particularly characteristic functions.

2.1. Cell Extensions

Neuroblastoma cells form extensions that resemble nerve fibers[18-20,28-33]. The cells send these out under conditions that are unfavorable for cell multiplication, such as removal



(12)

of the serum from the culture medium[28,34,35], addition of bromo-[36,37] or fluorodeoxyuridine[19], 6-thioguanine[38], cytosine arabinoside[34], or dimethyl sulfoxide[39], production of a hypertonic medium[40], or X-ray irradiation[31]. Formation of such extensions has also been observed in the presence of nerve growth factor[41,42] or a factor produced from glial cells[43], of prostaglandin E_1 *(10)*[33], of dibutyryl cyclic AMP *(12)*[29,30][*], and of inhibitors of cyclic AMP-phosphodiesterase, *e.g.* papaverine[32].

2.2. Excitability of the Membranes

As a further function characteristic of nerve cells, neuroblastoma cells may contain excitable membranes. The excitation may be produced electrically[44,45] or chemically[46-48]. In the former technique a current pulse is sent through the plasma membrane *via* a microelectrode introduced into the cell (Fig. 2). The current is directed so that the interior of the cell,

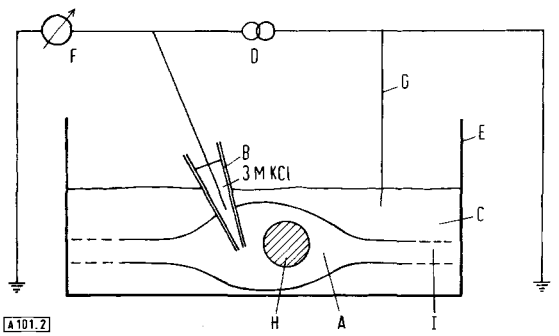


Fig. 2. Principle of the electrophysiological investigation of a single cell in culture. The cell (A) (diameter 0.01 to 0.1 mm) is penetrated by a microelectrode (B). The electrode is a conical glass capillary filled with 3 M KCl, the diameter of its point being less than 1 µm. The potential between the cell interior and the growth medium (C) (which is at ground potential) is called the membrane resting potential, and is generally about −50 mV. This potential can be artificially raised by an external potential source (D) to a value at which, within a few milliseconds, the permeability of the membrane to specific ions is changed dramatically (action potential). The cell and the microelectrode are drawn much too large in relation to the culture dish (E). F = voltmeter (oscilloscope), G = reference electrode, H = cell nucleus, I = cell extension (axon).

which is negatively charged with respect to the medium, is depolarized to a less negative potential; membrane excitation spreading over the cell surface is thereby produced, *i.e.* an action potential. In chemical excitation acetylcholine, which acts as a transmitter at the connections between motor nerves and muscles, is metered out from a micropipette onto the cell surface iontophoretically by short current pulses.

2.3. Neurohormone Receptors

Neurotransmitters can introduce an action potential only if the target cells have appropriate receptors on their surface. On binding to these receptors, neurotransmitters and other neurohormones such as morphine can also produce other effects: they may activate the enzymes adenylate cyclase[49,50] or guanylate cyclase and thus cause an increase in the intracellular concentration of cyclic AMP[51-55] or cyclic GMP[56-60] (Fig. 3). The cyclic nucleotides probably act as intracellular mediators (second messengers) of extracellular hormones[61]

[*] Abbreviations: cyclic AMP = adenosine 3',5'-cyclic monophosphate; cyclic GMP = guanosine 3',5'-cyclic monophosphate; dibutyryl cyclic AMP = N^6,$O^{2'}$-dibutyryladenosine 3',5'-cyclic monophosphate.

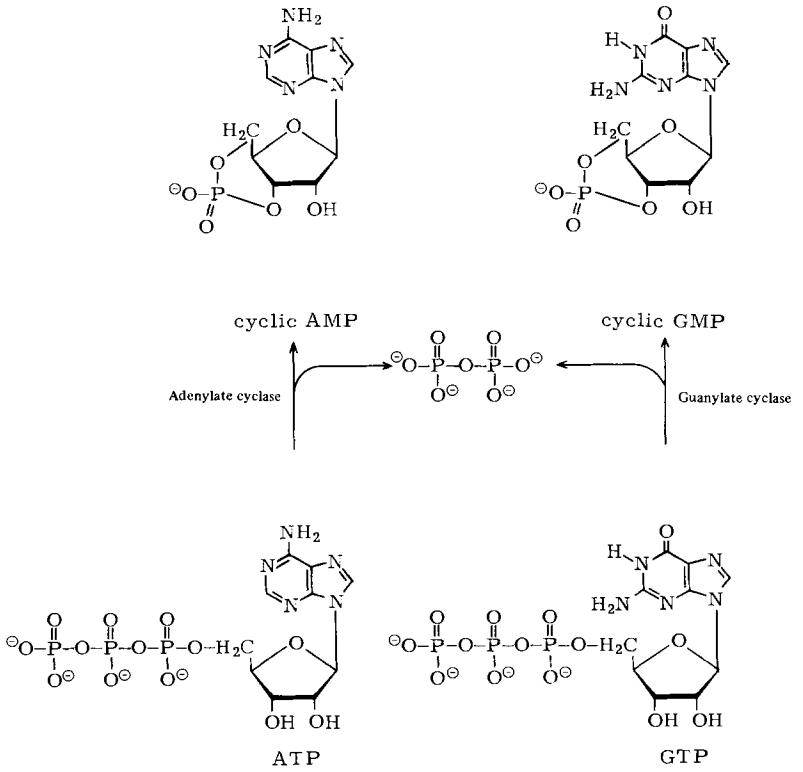


Fig. 3. Formation of cyclic AMP from ATP by the enzyme adenylate cyclase and formation of cyclic GMP from GTP by guanylate cyclase.

This, however, has so far been shown conclusively only for cyclic AMP[62]

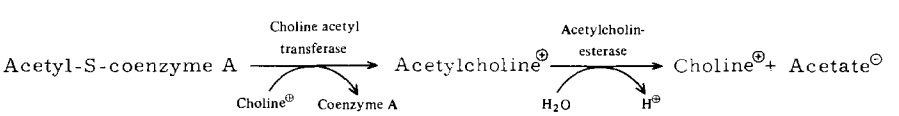
To detect receptors for neurotransmitters (and other hormones) one can also measure the specific binding of radioactively labeled neurotransmitters or their analogs or competitive inhibitors (antagonists) on the plasma membrane. Antagonists are usually favored for such studies because of their high binding constants (which are due to the low dissociation rate constants); the polypeptide α-bungarotoxin isolated from snake venom is such an antagonist for acetylcholine. Nevertheless, binding of α-bungarotoxin to neuroblastoma cells has so far been found possible in only one laboratory[63].

2.4. Transport Systems for Neurotransmitters and Their Precursors

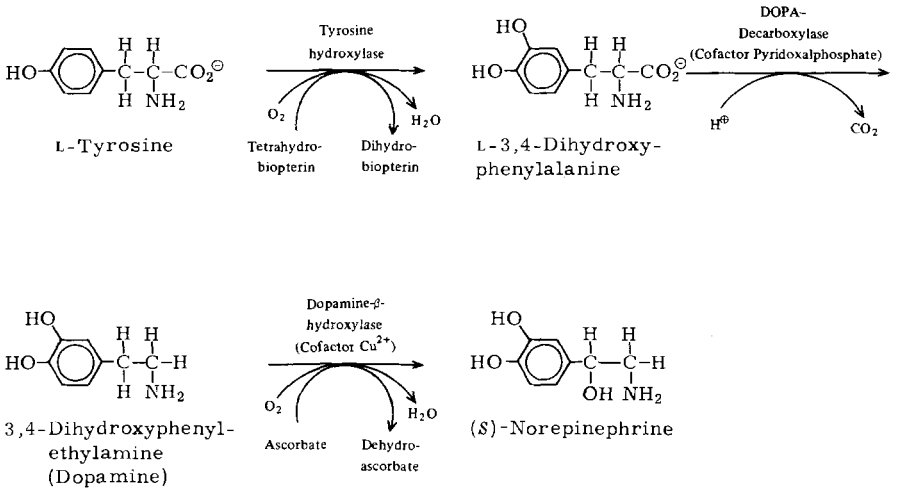
In order to excite the plasma membrane of the postsynaptic cell, the neurotransmitter ejected from the presynaptic nerve cell must be rapidly removed from the synaptic gap; failing this, it accumulates there and transfer of new information by the neurotransmitter becomes impossible. Its removal can be effected in two ways. In the first case the neurotransmitter in the synaptic gap may be changed by enzymes bound to the membrane, *e.g.* cleaved. The best example of this is the inactivation of acetylcholine *(1a)* by hydrolysis in the presence of the enzyme acetylcholinesterase; the choline formed is probably taken up by the surrounding cells (neurons, glia), most of it presumably by the presynaptic cells that had released the acetylcholine. In the second case the removal occurs by reuptake alone; this occurs *e.g.* for norepinephrine *(2b)*, serotonin *(3)*, and histamine *(4)*, and one can thus consider the transport systems for choline and norepinephrine as "differentiated properties" of cells of the nervous system. Neuroblastoma cells also possess such transport systems for choline[64,65], dopamine *(2a)* and norepinephrine[66,67], γ-aminobutyrate *(7)*[68,69], glycine *(6)*[27,70], and taurine *(8)*[70].

2.5. Enzymes Synthesizing Neurotransmitters

Like nerve cells, neuroblastoma cells have the ability not only of reacting to neurotransmitters but also themselves synthesizing such information carriers. They may contain the enzyme choline acetyltransferase [EC 2.3.1.6][18,22,24,71-75] which catalyzes the biosynthesis of acetylcholine (Scheme 1). Other neuroblastoma cells contain the enzyme tyrosine hydroxylase [EC 1.14.3.a][18,22,74,76,77] and dopamine β-hydroxylase [EC 1.14.2.1][78-80], which take part in the synthesis of the dopamine and norepinephrine found in the cells[81-83] (Scheme 2).



Scheme 1. Biosynthesis and hydrolysis of acetylcholine.



Scheme 2. Biosynthesis of dopamine and norepinephrine.

3. (Neuroblastoma × Glioma) Hybrid Cells

3.1. Preparation of the Hybrids

The formation of multinuclear cells by fusion of single cells was known already in the 19th century. In 1960 *Barsky et al.*[84] observed that cells of various mouse strains fuse spontaneously during culture to give hybrid cells whose nuclei contain chromosomes of both parent cells. *Harris* and *Watkins*[85] made use of *Okada*'s observation[86,87] that Sendai virus (a parainfluenza virus) fuses cells to form multinuclear giant cells in high yield, and even united cells of different species, such as man and mouse, by this method. The resulting multinuclear cells are called heterokaryons. Such cells occasionally divide, forming chromatin spindles common to the chromosomes of all nuclei. The resulting daughter cells then contain only one nucleus, this having the chromosomes of both parent cells; they are thus called hybrid cells (Fig. 4). If two cell lines mutated at different enzyme-coding gene positions are used for such hybridization[88], they complement each other in the hybrid to form a wild type[88]. It is then

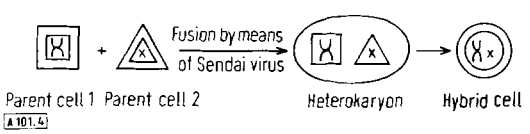


Fig. 4. Scheme of cell hybridization. The difference between the parent cell lines is symbolized by their different shapes. The internal small squares, triangles, and circles represent the cell nuclei. The internal X-shaped structures denote two different types of chromosomes.

only necessary to select in favor of the wild type rather than the mutant in order to obtain a wild-type-like population of hybrid cells. More or less homogeneous cell lines can be obtained by cloning these hybrid cells.

Fusion of a mouse neuroblastoma line (N4TG3 or N18TG2[89-92]) with a glioma line derived from a rat glial tumor (C6-BU-1) gave hybrid cells containing surprisingly high choline acetyltransferase activity; this activity was very low or nonexistent in the parent cells.

The (N18TG2 × C6-BU-1) hybrid clones 108CC5 and 108CC15 in particular have properties of neurons. They will be discussed first below in order to show that they can be regarded as models for nerve cells; it will be demonstrated by two examples how such cells can be studied as models for those cell problems that can be investigated only with difficulty by other methods.

3.2. Neurotransmitter Enzymes

The activity of the choline acetyltransferase can be controlled. It depends strongly on the cell density in the culture and can be increased by culturing the cells in the presence of dibutyryl cyclic AMP *(12)* to values such as are found in brain homogenates[91,92]. The hybrid cells cannot synthesize either dopamine *(2a)* or norepinephrine *(2b)* from tyrosine, because they contain no tyrosine hydroxylase which is the first enzyme in this biochemical pathway (see Scheme 2). The third enzyme of this process, namely dopamine β-hydroxylase, is however present[80].

3.3. Differentiation of Hybrid Cells

If the (neuroblastoma × glioma) hybrid lines 108CC5 or 108CC15 are exposed to a growth medium 1 mM in dibutyryl cyclic AMP *(12)*, their reproduction rate decreases greatly and they begin to differentiate[80,91-93]. In one or two weeks the cells, previously mostly round (Fig. 5A), send out long extensions (Fig. 5B—D). Like the axons of normal nerve cells, these extensions contain fibrous structures, namely 100 Å-long filaments and bundles of microtubules as well as "clear" and "dense-core" vesicles (Fig. 1) with diameters of 500—700 and 2000—3000 Å respectively[93]. The clear vesicles resemble the acetylcholine-storage vesicles of cholinergic nerve endings, but it is not yet known whether in the case of the hybrids they contain the acetylcholine formed in the cells. The dense-core vesicles resemble those of adrenergic nerve cells of the sympathetic nervous system; there they contain, *inter alia*, norepinephrine, the energy-storing substance adenosine triphosphate, and dopamine β-hydroxylase (Scheme 2); we presume that this enzyme is also localized in the dense-core vesicles of the hybrids; the vesicles of the hybrid cells cannot contain norepinephrine, since the first enzyme shown in Scheme 2 for this synthesis chain is missing (see Section 2.5).

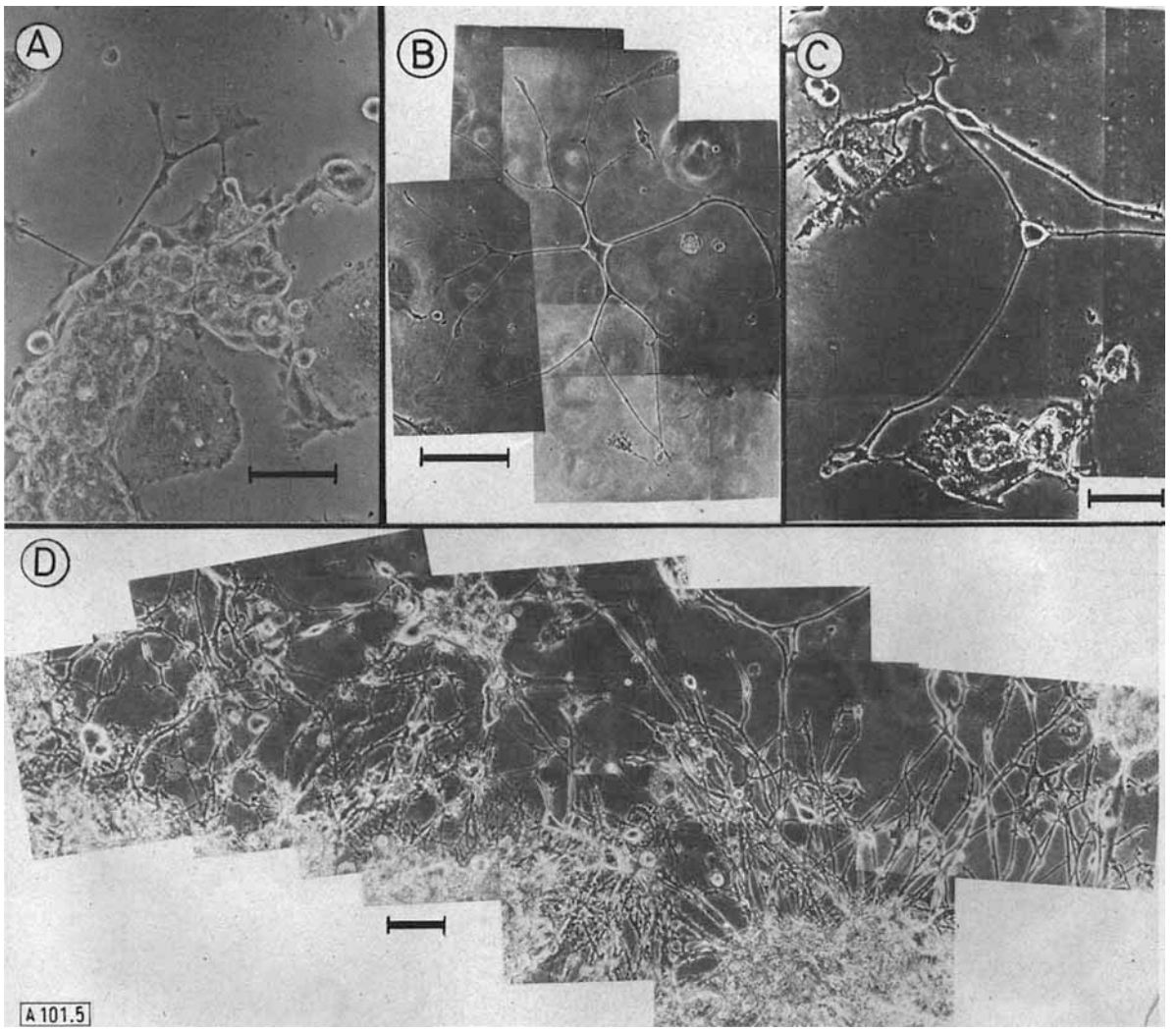


Fig. 5. A: Normal self-replicating (undifferentiated) (neuroblastoma × glioma) hybrid cells 108CC5. B—D: Hybrid cells differentiated by treatment with dibutyryl cyclic AMP. Pictures A [80] and B [80, 91] are reproduced from earlier publications. Scale: 100 µm.

3.4. Electrical Excitability and Cations

If a depolarizing electric pulse is allowed to flow through the plasma membrane of a differentiated hybrid cell by means of a microelectrode placed in the cell interior (Fig. 2), the cell releases an action potential that can be recorded by means of the same electrode (Fig. 6)[91]. The increasing phase of the action potential is generally derived from a passive inflow of Na^+ ions into the cell and the falling phase from a passive outflow of K^+ ions[94].

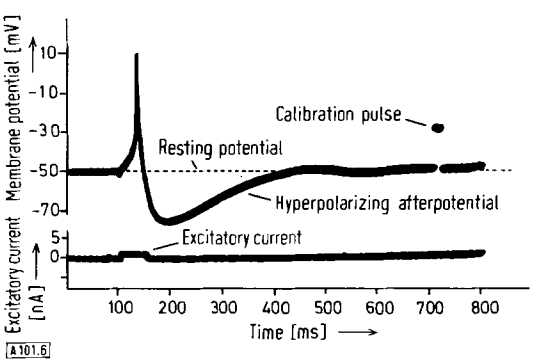


Fig. 6. Oscilloscope traces of an action potential triggered off by a depolarizing excitatory current through the plasma membrane of a hybrid cell 108CC5. Upper trace: membrane potential. A reference pulse of 20 mV and 20 ms duration appears after the action potential. Lower trace: depolarizing current 1 nA and 50 ms [91].

The inflow of Na^+ ions into the hybrid cells can be inhibited by tetrodotoxin, the poison of the Japanese globefish[95]. However, if the Ca^{2+} concentration in the medium is increased, dramatic changes in the electrical properties are observed[91, 95]:

1) Tetrodotoxin no longer inhibits the action potential.
2) Cells that previously had a weakly developed action potential (Figs. 7A, C) now have a well developed one (Fig. 7B) and often respond to a single depolarizing excitation pulse with hundreds of action potentials (Fig. 7D).
3) The excitation threshold for the release of an action potential by an electric pulse or by acetylcholine is greatly lowered.
4) The hyperpolarizing afterpotential of the cells (Figs. 7B, D), which follows on the falling branch of the action potential, is enormously increased.

The insensitivity of the action potential to tetrodotoxin indicates that with an increased Ca^{2+} concentration the inward flow must be of Ca^{2+} and not of Na^+ ions. This assumption was correct because action potentials can also be obtained in the absence of Na^+ provided that sufficient Ca^{2+} is present. Furthermore, these action potentials can be inhibited by the

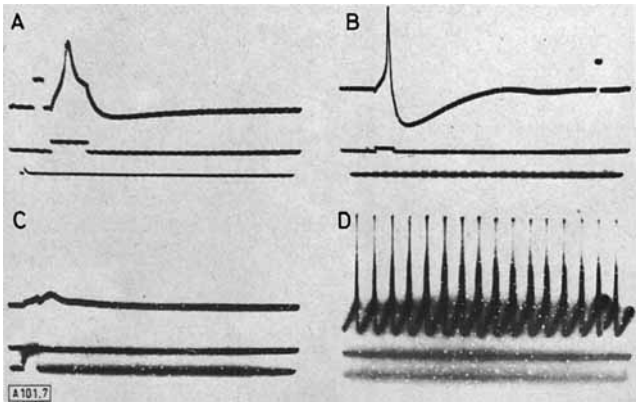


Fig. 7. Effect of increasing the Ca^{2+} concentration in the external medium on the action potential of hybrid cells 108CC15 (A, B) and 108CC5 (C, D). Oscilloscope traces A and C before, and B and D after, the addition of 10 µl (B) or 20 µl (D) of 0.5 M $CaCl_2$ to the medium above the cell under study. D: A single acetylcholine pulse produced a series of more than 200 action potentials, some of which are shown [91].

Ca^{2+} antagonists Co^{2+}, Mn^{2+}, Mg^{2+}, and La^{3+} as well as by organic inhibitors of the Ca^{2+} inflow[95]; the activity and specificity of these substances was proved on other systems having Ca^{2+}/K^+ action potentials.

3.5. Electrical Excitability and Receptors

Action potentials are released if acetylcholine is metered out iontophoretically onto the surface of differentiated hybrid cells[91]. These potentials migrate over the surface of the entire cell. The action of the acetylcholine can be inhibited reversibly by atropine or D-tubocurarine, and irreversibly by α-bungarotoxin[91]. As with skeletal muscle fibers, so with these hybrids high doses of acetylcholine cause transient insensitivity to further acetylcholine[91].

Norepinephrine and morphine[57], as well as dopamine[96,97], also depolarize (Fig. 2) the hybrid cells and trigger off action potentials, whereas prostaglandin E_1 increases the membrane potential (hyperpolarization)[57].

3.6. Neurohormones and Cyclic Nucleotides

Prostaglandins, like cyclic nucleotides, occur in all animal tissues and thus also in the nervous system. They are formed enzymatically from dihomo-γ-linolenic acid or from arachidonic acid. They appear to exert their action locally, *i.e.* in the neighborhood of the cells that produce them. In accord with the functions of the various organs, they influence a considerable number of different processes in the organism[98–101]. A change in the intracellular level of cyclic nucleotides could be one common denominator of the diverse prostaglandin actions. Prostaglandin E_1 *(10)* increases the intracellular concentration of cyclic AMP in the hybrid cells 50- to 100-fold in 10 min[102–105]. Fig. 8 shows that the half-maximal effect occurs at a 20 nM concentration of PGE_1[103].

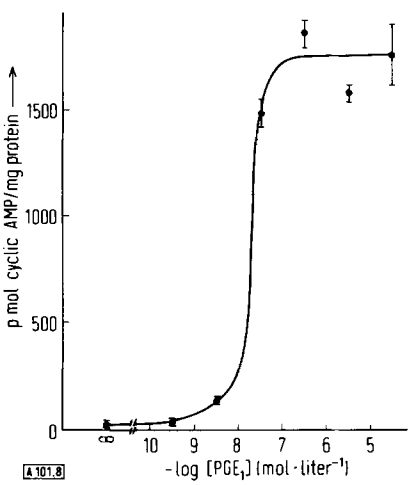


Fig. 8 Dependence of the intracellular concentration of cyclic AMP on the PGE_1 concentration in the medium. Replica plastic dishes containing hybrid cells 108CC15 were incubated for 10 min at 37 °C with increasing concentrations of PGE_1 and then analyzed for their cyclic AMP content [103].

If the cells are incubated with the maximal stimulating concentration of PGE_1 and increasing concentrations of acetyl-

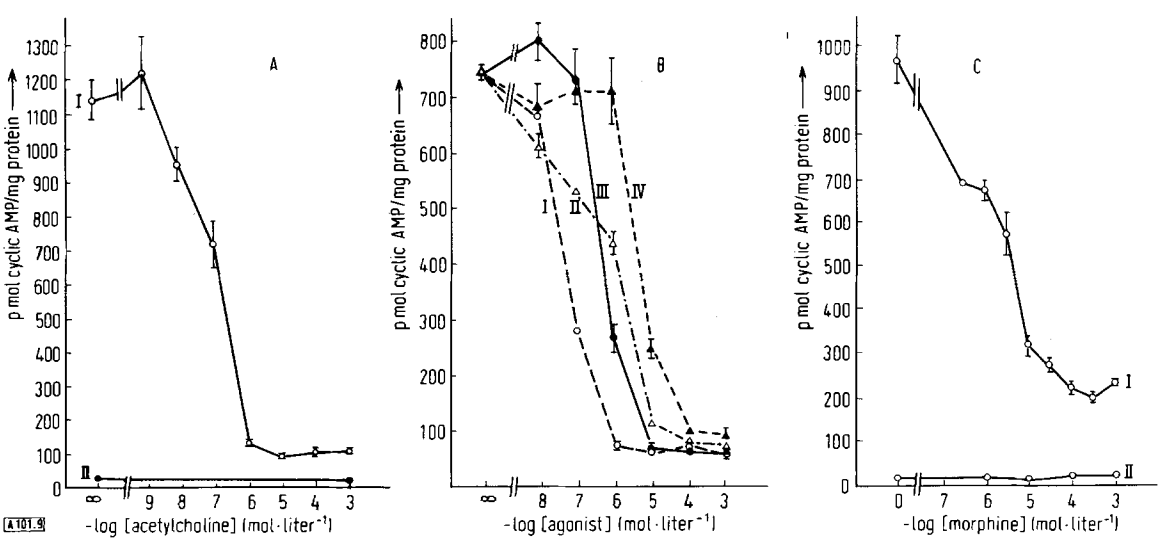
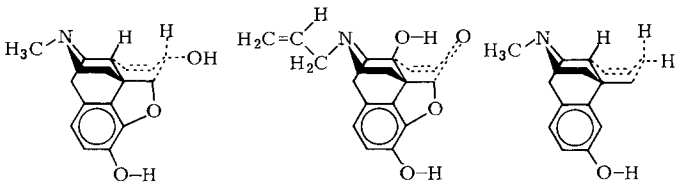


Fig. 9. Inhibition of the increase caused by 3 µm PGE_1 in the level of cyclic AMP in hybrid cells 108CC15 on treatment with acetylcholine (A) [56], adrenergic agonists (B) [57], and morphine (C) [104].—A, curve I: presence of PGE_1; curve II: absence of PGE_1.—B: All experiments in the presence of PGE_1, curve I: norepinephrine *(2b)*; II: phenylephrine *(2d)*; III: dopamine *(2a)*; (IV): isoproterenol *(2c)*.—C, curve I: presence of PGE_1; curve II: absence of PGE_1.

choline[56] (Fig. 9A), or of adrenergic neurotransmitters (agonists) such as norepinephrine[57] (Fig. 9B) or with morphine *(13)*[104] (Fig. 9C), then most of the increase in the level of cyclic AMP does not occur. The action of the acetylcholine (Fig. 9A) can be inhibited by atropine, but not by D-tubocurarine, which indicates the presence of a muscarinic but not of a nicotinic acetylcholine receptor of the hybrid cells[56]. From the fact that norepinephrine *(2b)* is effective at a much lower concentration than isoproterenol *(2c)* it can be concluded that an adrenergic α- but not a β-receptor is present. The results of experiments with specific norepinephrine antagonists support this conclusion[57]. The effect of morphine can also be prevented by a specific inhibitor, naloxone *(14)*[104]. Each inhibitor only prevents the action of the appropriate agonist; thus, naloxone does not inhibit the action of acetylcholine or of norepinephrine[103]. From this and other investigations[106] we conclude that all the receptors of hybrid cells are different molecules. Today there is no doubt that they are proteins[107]. Substances with morphine-like activity, such as levorphanol *(15)*, methadone, heroin, and meperidine, also behave like morphine in hybrid-cell systems[103].



(13) *(14)* *(15)*

The inhibitory action of acetylcholine, norepinephrine, and morphine is not confined to the increase in the level of cyclic AMP produced by PGE_1. Adenosine *(11)* and isobutylmethylxanthine, like PGE_1, increase the cyclic AMP concentration in the hybrid cells[108, 109], the former by increasing the rate of synthesis and the latter by blocking degradation. In both cases the increase in the level of cyclic AMP is hindered by acetylcholine[56], norepinephrine[57], or morphine. From this it is concluded that all three substances decrease the level of cyclic AMP by reducing the rate of synthesis. In agreement with this, measurements of the adenylate cyclase activity of hybrid-cell homogenates have shown that morphine prevents the increase in this activity by PGE_1[110].

These discussions permit two problems to be recognized, to whose solution hybrid cells can contribute:

1) The processing of information reaching a cell in the form of antagonizing hormonal signals.

2) The mechanism of the action of opiates.

Below we shall turn our attention successively to these two questions.

3.7. Biochemical Processing of Hormone-Borne Information

The physiological effects of hormones that increase the cellular level of cyclic AMP are in opposition to those caused by hormones that increase the level of cyclic GMP[111]. Following a proposal by *S. Cha, N. D. Goldberg et al.* considered this dualism to be analogous to the ancient mutually contradictory Chinese principles of Yin and Yang[112, 113]. Our presumption in agreement with these concepts was confirmed by the fact that the decreases in the levels of cyclic AMP caused by acetylcholine, norepinephrine, or morphine and its analogs should be accompanied by increases in the levels of cyclic GMP[58, 59, 114]. Surprisingly, the increase

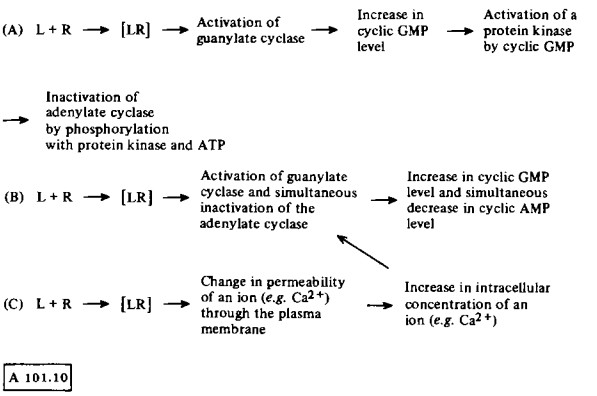


Fig. 10. Three hypotheses for the activation of the guanylate cyclase activity and inhibition of adenylate cyclase activity by binding of the ligands L (acetylcholine, norepinephrine, or morphine) to their receptors R.

in the level of cyclic GMP is of only very short duration. Thus, the maximum of the level of cyclic GMP in the presence of carbamoylcholine *(1b)*, a synthetic analog of acetylcholine, is reached already after 1 min. After about 10 min the values can be back to the original level[58]. Similar observations have been made for norepinephrine and morphine[59]. In all cases the concentrations of cyclic AMP and cyclic GMP take opposing courses. If the level of the former sank below its original value then that of the latter rose above its original level, and *vice versa.*

How can one picture the molecular mechanism of these opposing regulations? On what plane do they occur? Fig. 10 presents three hypotheses. Other groups of investigators came to similar views[115–117]. Further experiments with hybrid cells are required for a decision between these possibilities.

It is striking that acetylcholine, norepinephrine, and morphine, which increase the level of cyclic GMP, have a depolarizing action on the hybrid-cell membrane, whereas PGE_1, which raises the level of cyclic AMP has a hyperpolarizing effect[57]. Similar relationships between PGE_1 and norepinephrine have been found for brown fat cells[118]. These parallels permit the assumption either that depolarization of the cell membrane and activation of the guanylate cyclase on the one hand and hyperpolarization and activation of the adenylate cyclase on the other are linked causally, or that they have a common origin.

Furthermore, it seems important that in hybrid cells the substances acetylcholine, norepinephrine, and morphine which raise the level of cyclic GMP can overcome (*i.e.* dominate) the action of the compounds PGE_1 and adenosine which raise the level of cyclic AMP. The decision between the three hypotheses set out in Fig. 10 is also likely to provide evidence concerning the dominance of the guanylate cyclase system over the adenylate cyclase system.

3.8. Investigations of the Action of Morphine

3.8.1. The Acute Action of Morphine

The contraction of the smooth muscles of the small intestine produced by PGE_1 is inhibited by morphine[119–121]. Since

PGE_1 increases the level of cyclic AMP in neuroblastoma[51, 52] and hybrid cells[102], it became desirable to test whether morphine would also suppress the action of PGE_1 in this system. Experimentally, in intact neuroblastoma[104, 106, 122] and (neuroblastoma × glioma) hybrid cells[106] (Fig. 9C) morphine hinders the increase in the levels of cyclic AMP caused by PGE_1 and inhibits the stimulation of adenylate cyclase by PGE_1 in hybrid-cell homogenates[110] or rat-brain homogenates[123]. The presence of morphine receptors was established not only by these indirect methods but also directly by stereospecific binding of radioactive dihydromorphine to intact neuroblastoma and hybrid cells[105].

The next question is whether *all* cells in which the level of cyclic AMP increases in the presence of PGE_1 react to morphine. Rat glioma cells and (rat glioma × mouse fibroblast) hybrids are elicited by PGE_1 to form cyclic AMP[102]; in no case does morphine inhibit this process[106]. These experiments show that the receptors for PGE_1 and morphine are present independently of one another, and the question just raised must thus be answered in the negative. Since inhibition of the PGE_1 action by morphine is not competitive[102], *i.e.* since PGE_1 and morphine do not compete for the same binding site, the PGE_1 and morphine receptors are not identical. The action of morphine is independent of that of PGE_1. Whatever agent is used to increase the level of cyclic AMP, morphine inhibits that effect[108] insofar as morphine receptors are present.

The inhibiting effect of opiates on the increase in the level of cyclic AMP by PGE_1 in neuroblastoma and hybrid cells is stereospecific. Levorphanol *(15)*, which behaves like morphine in animal experiments, also acts like morphine in the cell system, whereas dextrorphan, which is an enantiomer of levorphanol and inactive in the animal, has no effect on

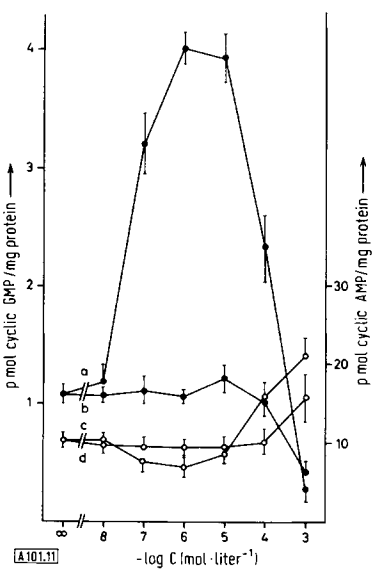


Fig. 11. Influence of the concentration of levorphanol and dextrorphan on the level of cyclic GMP and cyclic AMP in hybrid cells. The cells were incubated for 10 min with levorphanol (curves a and c) or dextrorphan (curves b and d). Curves a and b: cyclic GMP; curves c and d: cyclic AMP [114].

the cell system[57, 110]. Naloxone *(14)* is a morphine antagonist used in cases of morphine poisoning; it has no opiate action itself, although the structure contains the morphinan skeleton. In cell cultures too naloxone inhibits the action of morphine[104, 105]. As mentioned in Section 3.6, an increase in the level of cyclic GMP occurs alongside a decrease in the level of cyclic AMP[114]. Opiates act stereospecifically not only when they decrease the level of cyclic AMP but also when they raise the level of cyclic GMP; levorphanol *(15)*, but not dextrorphan, acts like morphine (Fig. 11, curves a and b). The effect of levorphanol is maximal in the concentration region of 1 to 10 μM (Fig. 11, curve a); at higher concentrations there is a smaller increase, and finally a sharp fall in the level of cyclic GMP is observed; the fall in the level of cyclic GMP is paralleled by a rise in the level of cyclic AMP (Fig. 11, curve c). The importance that cyclic GMP may have for the regulation of the level of cyclic AMP was discussed in Section 3.7.

Neuroblastoma cells and—because of their greater sensitivity to morphine and neurohormones[56, 104, 110]—especially hybrid cells are thus useful models for investigating the biochemistry involved in the action of morphine. It is well known that analgesia is the medicinally important acute action of morphine. On the basis of the studies with model systems it can be assumed that an increase in the level of cyclic AMP is responsible for the feeling of "pain" in the neurons important for registration of pain and that a decrease in the level of cyclic AMP is thus correlated with a decrease in pain or even a strong sensation of well-being.

Like the neurotransmitters acetylcholine and norepinephrine, morphine inhibits the rise in the level of cyclic AMP caused by PGE_1 and increases the level of cyclic GMP. Is morphine then a neurotransmitter? The answer must be "No", because morphine is not formed in the animal body. Morphine could, however, imitate an endogenous neurotransmitter, and in fact this has meanwhile been proved by several groups of investigators. "Endogenous morphine" (endorphine) is a small peptide[*] with a relative molecular weight of 1000 to 2000[124–130]; partially purified endorphine also has morphine-like action in the hybrid-cell system[131]. Furthermore, there is evidence that the hybrid cells produce one or more factors behaving similarly to morphine[132]. An analogy between the action of norepinephrine and that of morphine is also found in the intact animal: when injected into the brain of rats, norepinephrine, like morphine, has an analgesic effect[133]. Naloxone, a morphine antagonist, does not inhibit the effect of norepinephrine. Thus, it can be presumed that norepinephrine does not act indirectly by causing a release of endorphine.

3.8.2. Chronic Action of Morphine; Morphine Tolerance, Dependence, and Withdrawal

Following long-term action of morphine on hybrid-cell cultures some phenomena are observed that can be treated as biochemical correlates of morphine tolerance, dependence, and withdrawal[134, 135]. After at least 15 h of preincubation of hybrid cells with morphine, subsequent main incubation (10 min) with PGE_1 (in the absence of morphine) causes the

[*] *Note added in proof* (April 2, 1976): Meanwhile two such peptides, called enkephalin, have been analyzed and synthesized. Their sequences are H-Tyr-Gly-Gly-Phe-Leu-OH and H-Tyr-Gly-Gly-Phe-Met-OH (*J. Hughes, T. W. Smith, H. W. Kosterlitz, L. A. Fothergill, B. A. Morgan,* and *H. R. Morris*, Nature *258*, 577 (1975)). Synthetic enkephalin shows acute and long-term morphine-like actions on the hybrid cells (*M. Brandt, R. J. Gullis, K. Fischer, C. Buchen, B. Hamprecht, L. Moroder,* and *E. Wünsch*, to be published).

level of cyclic AMP to reach about twice the value it had before the preincubation with morphine (Fig. 12, curve a)[134].

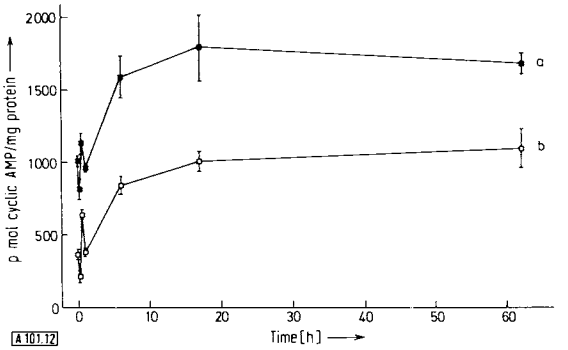


Fig. 12. Time course of the development of the response to PGE_1 during pretreatment of the hybrid cells with 10 μM of morphine. After preincubation times shown by the experimental points the cells were washed and then incubated for 10 min at 37°C with 3 μM of PGE_1 (curve a) or 3 μM of PGE_1 + 100 μM of morphine (curve b) before the content of cyclic AMP in the cells was measured [134].

If, however, the morphine is omitted during the preincubation the reaction of the cells to PGE_1 does not change. After any length of preincubation with morphine (between 0 and 62 h) the effect of the PGE_1 on the level of cyclic AMP is always inhibited by morphine (Fig. 12, curve b).

We regard the hybrid cells as a model of morphine-sensitive cells in the brain. Suppose that the level of cyclic AMP shown by the first experimental point on curve a in Fig. 12 corresponds to the normal finding for man or animal, and that the first experimental point on curve b corresponds to the feeling of special well-being that follows the use of morphine. We can then assume that an increase in the level of cyclic AMP denotes a decrease in the well-being rising to markedly unpleasant sensations. If after chronic administration of morphine and subsequent withdrawal of the drug a constant amount of PGE_1 causes a level of cyclic AMP greater than before the treatment with morphine, this denotes increased ill-feeling (Fig. 12, curve a, *e.g.* $t = 18$ h). Ill-feeling can be converted into a feeling of normality by administration of morphine

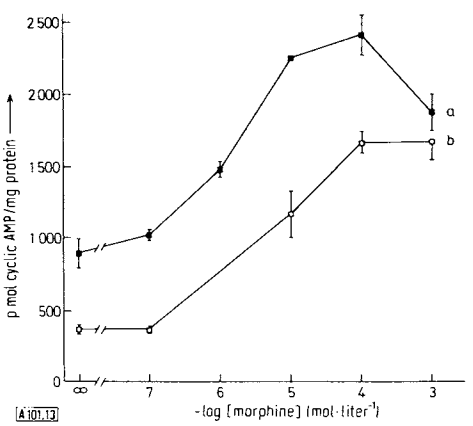


Fig. 13. Relation between the response to PGE_1 and the morphine concentration during a preincubation period of 15 h. After the preincubation the cells were treated as described in Fig. 12.

(transition from curve a to curve b, for example at $t = 18$ h). To produce a pronounced feeling of well-being an amount of morphine must now be taken that exceeds that required at, *e.g.* $t = 0$ (morphine tolerance). Conversely, the transition from curve b to curve a at, *e.g.*, $t = 18$ h corresponds to a withdrawal syndrome. Development of an increased response to PGE_1 depends on the morphine concentration during the preincubation period (15 h) (Fig. 13). The occurrence of morphine tolerance in hybrid cells is hindered by cycloheximide, which is an inhibitor of protein biosynthesis[132, 134]. Such inhibitors also prevent the formation of morphine tolerance in animals[136–138]. We know nothing about the nature of the proteins (*e.g.* adenylate cyclase?) whose synthesis is important for development of the tolerance phenomenon.

Since the short-term effects of acetylcholine and norepinephrine are the same as those of morphine (see Section 3.6), this analogy was also to be expected for the long-term effects. Because of the rapid degradation of acetylcholine *(1a)* and norepinephrine *(2b)* in cell cultures, their stable analogs carbamoylcholine *(1b)* and isoproterenol *(2c)* were used experimentally. Even after preincubation with these agents the hybrid cells showed greatly increased reaction to PGE_1 (Table 2)[134]. It follows that morphine, acetylcholine, and norepinephrine, as well as their analogs, produce the same long-term effects. This equality of action of the three substances does not hold after injection into an animal. Acetylcholine and norepinephrine are degraded in the periphery before they reach the brain. Also, both they and their analogs, unlike morphine, do not cross the blood-brain barrier; thus, they cannot pass on to the neurons. In addition, it should not necessarily be expected that morphine-sensitive cells in the brain possess also receptors for acetylcholine or norepinephrine. The experiments with model cells show that morphine does not occupy any special position and that tolerance can in principle be produced also by other substances.

Table 2. Effect of preincubation (36 h) of hybrid cells with various agents on the level of cyclic AMP that was found after the main incubation with PGE_1 [134].

Preincubation with 10 μM	Main incubation with 3 μM of PGE_1: cyclic AMP (pmol/mg protein)
	1310 ± 50
Morphine *(13)*	2540 ± 230
Carbamoylcholine *(1b)*	2560 ± 60
Isoproterenol *(2c)*	5620 ± 100

How is the short-term action of acetylcholine, norepinephrine, and morphine connected with their long-term action? On their application to the surface ot the hybrid cells the most important result is the binding of the ligands to their receptors. This acceptance, by the specific receptor, of information reaching the cell from outside corresponds to the uptake of information by a radio antenna tuned to a particular frequency. Binding of the ligand L to the receptor R (Fig. 14) presumably causes alterations in its structure that lead to changes in the membrane structure (ΔStr). These in turn result in changes in the ion permeabilities (Δg), which produce the first detectable event, namely an alteration of the membrane potential (ΔU) and of the intracellular ion concentration (ΔC_I). The changes in cyclase activity (ΔA) are noticed next by the change in the concentration of cyclic nucleotides (ΔC_{cNMP}). Finally, after many hours, one finds an increased response of the cells to PGE_1 (tolerance T). What is the course of the causal chain? Perhaps as in Fig. 14A, where a change

in the concentration of the cyclic nucleotide is a prerequisite for the appearance of the long-term effect T? Or as in Fig. 14B, where the change in the ion concentration C_I in the cell causes the long-term effect T, whereas the change in the

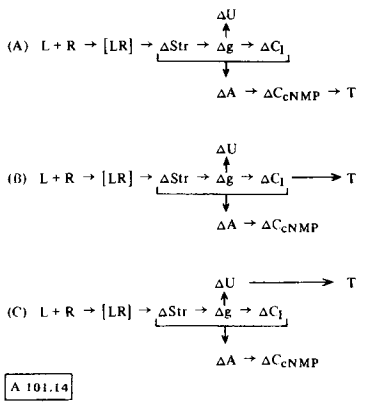


Fig. 14. Three hypotheses for development of the tolerance effect T on long-term action of opiates or cholinergic or adrenergic agonists. L: ligand (agonist). R: receptor. [LR]: ligand-receptor complex. ΔStr: structural alteration of the receptor and/or membrane. Δg: alteration of ion permeability. ΔC_I: alteration of intracellular ion concentrations. ΔU: alteration of the membrane potential. ΔA: alteration of the specific activity of cyclases. ΔC_{cNMP}: alteration of the intracellular concentration of cyclic nucleotides. T: tolerance.

level of cyclic nucleotides (ΔC_{cNMP}) is only a phenomenon running parallel to the development of T? Or as in Fig. 14C, where the change in the membrane potential provides the decisive impulse for development of the tolerance T? All three possibilities could be tested experimentally. In particular, it would seem interesting to exert an influence on ΔStr by changing the lipid composition of the membrane, which could be readily done for cell cultures.

4. Problems that Can Be Studied on the Hybrid Cell System

The first section of this review was devoted to the properties of neuroblastoma cells and of (neuroblastoma × glioma) hybrid cells, including their neuronal "luxury functions" (functions unnecessary for survival of the cells during culture). These characteristics are recapitulated in Table 3. The example

Table 3. Properties of (neuroblastoma × glioma) hybrid cells.

A) Neuronal characteristics:
Cell extensions (neurites)
Choline acetyltransferase
Dopamine β-hydroxylase
Clear vesicles (acetylcholine storage?)
"Dense-core" vesicles (norepinephrine storage?)
Action potential (excitable electrically or chemically)
B) Receptors [a] for:
Acetylcholine *(1a)*
Norepinephrine *(2b)*
Morphine *(13)* (endorphine)
Prostaglandin E_1 *(10)*
Adenosine *(11)*

[a] Insofar as the action of all the listed substances is transmitted through receptors. This list will probably be extended as a result of further findings.

of morphine action will now be used to show that problems almost insoluble by animal or tissue experiments can be brought nearer to solution by the use of model systems. For example, it is not yet possible to isolate specific regions of the brain so rapidly that the levels of cyclic nucleotides are not drastically altered during the isolation procedure, yet that would be essential for animal experiments with morphine of the type described above.

It is repeatedly asked whether the results obtained with cell cultures mirror events in the animal or in man, so that they can be applied to the normal organism. This question is justified, for the culture cells are separated from the surrounding tissue constituents and exist in an environment whose chemical composition may differ in important ways from that in the tissue. In addition, tumor and hybrid-cell lines in particular contain chromosome populations that are not whole-number multiples of a simple chromosome set (aneuploidy); their chromosome number ranges from cell to cell around a mean value. Nevertheless, these cells contain no new information in their genome beyond that present in "normal" cells. It is currently assumed that there is no information in a genome beyond that necessary somewhere in the organism; if that were not so, it would have been eliminated during evolution. If this is correct, then all the molecular functions observed in cell systems must also occur in the animal body at some time and in some place. The environment and aneuploidy can then produce only quantitative, and not qualitative, deviations from the state normal in the animal.

It will always be difficult to correlate a model cell with a specific cell in the body, since the model cell may be unique in its combination of phenotypic characteristics. Such a correlation is, however, not necessary. One chooses a type of model cell simply because it provides the best basis for studying the properties of interest, and the other characteristics presented by it need not necessarily interfere. Hybridization of other permanent neuronal cell lines with one another, or of a permanent cell line with isolated neurons, will probably permit new cell lines containing new combinations of characteristics to be produced; experiments in this direction are in progress[139]. The results of cell-culture experiments must be tested on the intact organism.

Because of the homogeneity and often almost unlimited replicability of cultivated cell material, serial experiments can be carried out, as in bacteriology, with replica cultures. However, cell culture systems are reminiscent not only of the techniques of microbiology. It is pertinent to consider that neuroblastoma cells may be the *Escherichia coli* of neurobiology[26]: animal experiments can be carried out on the basis of experiments with cell cultures in a more controlled manner than is otherwise possible. Behavior of cell cultures that deviates from the norm for the intact tissue need not be a disadvantage. On the contrary, it has already led to the discovery of new regulatory hormone-like factors[140].

Table 4 lists problems for whose solution model systems such as (neuroblastoma × glioma) hybrid cells may, we believe, be helpful. At the head of the list is that most important of the functions of the nervous system, namely memory, and the brief discussion below concerns only that aspect. As described above, cells "remember" in long-term experiments the influence of cholinergic and adrenergic agents or of morphine. Also, the enormous transient increase in cyclic AMP phosphodiesterase activity after long-term incubation with PGE_1[108] can be interpreted as a memory function since, owing to the rapid degradation of cyclic AMP, the subsequent incubation with PGE_1 can effect only a slight increase in the level

of cyclic AMP. Naturally, great care is required here: one could regard every increase of enzyme activity in the liver after injection of hydrocortisone into an animal as the liver cells' "memory" of their "hormonal past". However, there is an important difference between neurons and liver cells: owing to the interconnection of the neurons one can "inquire" about the state of neurons that is altered under the influence of neurotransmitters and this information can be processed

Table 4. Problems that can probably be studied on hybrid cells by biochemical, cell-biological, pharmacological, and physiological methods.

1) Memory: storage, conservation, and recall of information
2) Synapses: formation (neuron-neuron, neuron-muscle, neuron-gland cell), function, cellular interaction
3) Differentiation: triggering and promoting factors (hormones), genesis of neurotransmitter storage vesicles, regeneration of nerve fibers
4) Intercellular communication: neurons with astroglia, neurons with axon-isolating Schwann cells
5) Neurotropic viruses [141]: virus diseases of the nervous system, "slow viruses"
6) Drugs: mode of action, metabolism
7) Neuronal membranes: characteristic constituents, metabolism, influence of the lipid composition of the membrane on membrane functions (action potential, receptors), lipid-protein interaction
8) Neurotransmitters: regulation of the formation and degradation, mechanism of reabsorption
9) Nutrition: influence of the supply of amino acids, sugars, and lipids on the development and function of neurons and glial cells
10) Trophics: controlled growth of nerves, controlled migration of neurons and glial cells
11) Axoplasmic transport
12) Cell movement (pulsation)
13) Constituents of the nervous system with known structure but unknown function

further in the brain. In the most unfavorable case experiments with hybrid cells could show what memory is not, and thus lead indirectly to its clarification.

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A Synthesis of Prostaglandins: Strategy and Reality[**]

By Ivan Ernest[*]

The prostaglandin synthesis developed in the Woodward Research Institute at Basel serves to provide an unusual look behind the scenes. A candid account is presented of the sometimes tortuous chronological sequence of ideas and experiments during work on a challenging synthesis.

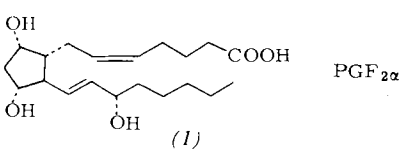
1. Introduction

Fortunately or not, the sober and dispassionate form of today's scientific publications does not leave much room to express or even suggest the creative motivation and atmosphere in which ideas originate and are further developed. To fill that gap with at least one example and in the hope that such an unusual presentation may have a beneficial effect a full insight into the process of design and development of a "classical" synthesis is given in the following paragraphs. For that purpose, our choice fell upon the synthesis of prostaglandins accomplished not long ago in the Woodward Research Institute at Basel. The synthesis, already published as a preliminary communication[1], will not now be presented in the conventional form, *i. e.* as if every step in the final version were foreseen from the very beginning, but rather as a sincere and more or less complete account of the chronological development of ideas and experimentation which finally led to the solution of the problem.

The prostaglandins are a large family of compounds with many promising pharmaceutical aspects: however, the multiplicity of physiological activities, so typical of the individual members, makes their medical application still somewhat problematic and the preference for any single compound very difficult.

Therefore any new synthesis had to be a general synthesis allowing a large-scale production of *any* desired natural prostaglandin. Moreover, it should provide an entry to as large a number of analogs as possible.

Fortunately enough, all known prostaglandins have closely related structures. This facilitates derivation of the common key intermediate for their synthesis. In such a case, the choice of key intermediate is guided by the structure of the most complicated member of the group to be synthesized: This approach maximizes the chance of synthesizing *all* members.



$PGF_{2\alpha}$

(1)

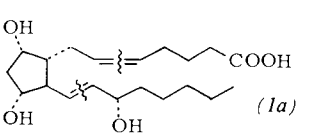
Formula *(1)* shows such a complicated representative of prostaglandins, *i.e.* $PGF_{2\alpha}$. It is not only one of the most interesting and most thoroughly studied members of the whole family from a physiological and medical point of view, but it also represents a great challenge to the synthetic chemist, combining in a single molecule most of the structural elements to be considered in the synthesis of any member of the group. Indeed, it has been shown that once a synthetic route to this compound had been found, the way was open to the other prostaglandins.

The structural challenges of $PGF_{2\alpha}$ are obvious. First there are the five chiral centers, four of them situated in a single cyclopentane ring, the remaining one forming part of a secondary, allylic alcohol grouping. Further, the reader will note two, mutually *trans* oriented, aliphatic side chains each with a double bond, one of which is *cis* disubstituted and isolated in a hydrocarbon chain of a fatty acid, and the other *trans* disubstituted and part of the allylic system in the other side chain of the molecule. The allylic hydroxyl is one of three secondary alcoholic groups, the other two being located, in a mutual *cis* orientation, in the five-membered ring.

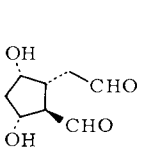
The accumulation of a relatively large number of stereochemical elements in a rather simple and poorly functionalized molecule decided the basic character of our synthesis: A highly stereospecific solution of the synthetic problem had to be found.

2. The Dialdehyde *(2a)* as Planned Key Intermediate (The "Cyclooctatetraene Approach")

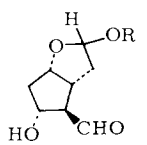
How was the structure of the common key intermediate of the synthesis to be described here derived from the structure of $PGF_{2\alpha}$? The dividing lines in *(1a)* suggest a dissection of the $PGF_{2\alpha}$ molecule at the sites of its double bonds in a kind of mental retro-Wittig reaction. By this imaginary operation, the prostaglandin structure falls apart into an interesting dialdehyde *(2a)* still containing four of the five chiral centers of $PGF_{2\alpha}$ and two side chain residues which—in the



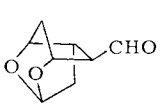
(1a)



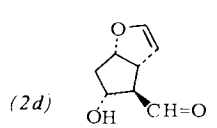
(2a)



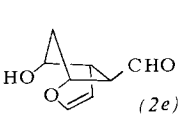
(2b), R = H, Alkyl



(2c)



(2d)



(2e)

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4002 Basel (Switzerland)

[**] Based on lecture presented at the "Symposium on Strategy in Organic Synthesis", Louvain-la-Neuve, March 1974.

synthesis—should be affixed to the above fragment by means of appropriate phosphorus ylides. The possibility of constructing the side chains of $PGF_{2\alpha}$ in such a way—an approach having obvious advantages for the synthesis of other prostanoids from the same key intermediate as well—was demonstrated before by *Corey*[2].

However, the famous Corey synthesis does not involve the dialdehyde *(2a)*, but rather a non-aldehydic key intermediate in which the aldehyde groups needed for the Wittig reactions are created separately in the further course of the synthesis immediately before each olefination, one by oxidation of a primary alcohol, which first has to be liberated from a protecting ether linkage, the other by reduction of a γ-lactone.

The idea of designing a synthetic scheme with *direct* formation of the dialdehyde *(2a)*, *i.e.* without the need for any additional oxidative-reductive transformations, was of course tempting. It was obvious that the "upper" aldehyde group, being part of a γ-hydroxy aldehyde system, would very probably exist as a hemiacetal [*(2b)*, R = H], form analogous cyclic acetals with alcohols [*(2b)*, R = alkyl], and might even be forced to enter into an interaction with both hydroxyl groups of the cyclopentane ring to form a tricyclic acetal *(2c)*. Similarly, two bicyclic enol ethers *(2d)* and *(2e)* could result from interaction of the above mentioned aldehyde group with one or the other hydroxyl function, respectively. In all these bi- or tricyclic structures, the two original aldehyde groups would be sufficiently differentiated—a prerequisite for the two Wittig reactions planned.

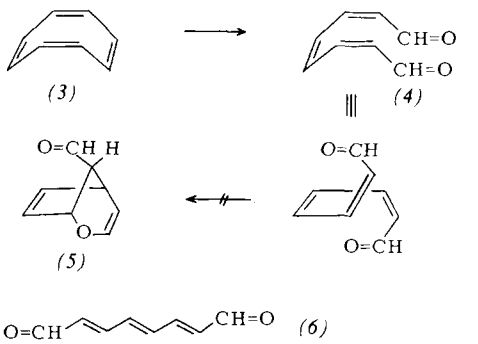
Thus, the dialdehyde *(2a)* or, more properly, its cyclic acetals or enol ethers, seemed to fulfill all the requirements of a good key intermediate:

Each one of these derivatives appeared to be universal for the entire prostaglandin group, as well as for a wide range of analogs;
in each case, most of the stereochemical problems of the synthesis would be solved;
each one of them bore the functions needed for the synthesis, either in their final form or in a form from which they are readily accessible;
they all complied with the useful principle of an internal and mutual protection of functional groups, which not only reduces the total number of synthetic steps and obviates the need for special protecting agents, but also makes the intermediate structures as simple as possible. Moreover, as will be shown later, the principle of mutual internal protection can serve the further purpose of providing excellent stereochemical control in the synthetic operations.

2.1. The Aldehyde *(5)* as Planned Precursor

It was initially proposed to derive a bicyclic, eight carbon atom structure *(5)*, which was very closely related to the desired ones, in two steps from readily available cyclooctatetraene *(3)*. A selective oxidative cleavage, *e.g.* ozonolysis, of one of the double bonds of this hydrocarbon should give all-*cis*-octatrienedial *(4)*, which in turn, in its spiral conformation, should undergo an internal Diels-Alder reaction. This reaction would provide the bicyclic system *(5)* with a cyclopentene ring bridged by an enol-ether grouping. The enol-ether bridge represents the acetaldehyde side chain and one of the hydroxyl groups of the key intermediate C_8-dialdehyde in a mutually protected form securing at the same time their desired *cis* orientation. The stereochemistry of the Diels-Alder reaction would further result in a *trans* orientation of the free aldehyde group to the enol-ether bridge—exactly as desired for our key intermediate. Thus, the five-membered ring of our key intermediate, three of its four chiral centers in correct configurations, three of its four functional groups directly in their proper functionalities, and an additional double bond for an easy introduction of the missing function, a hydroxyl group, would be created in one single step.

The literature supplied some encouraging data for this plan. There was an observation by *Wibaut* and *Sixma*[3] that on ozonization of cyclooctatetraene, the first mole of ozone is consumed faster than the following ones, thus suggesting the possibility of a selective cleavage of only one double bond. And there was a precedent for the Diels-Alder reaction between two unsaturated aldehydes in a cyclodimerization, under special conditions, of methacrolein[4].



In fact, ozonization of cyclooctatetraene at −78 °C with one equivalent of ozone in various solvents proved the correctness of the idea of a selective cleavage of one double bond, but, unfortunately, the experiments also suggested a very low stability of the resulting all-*cis*-dialdehyde *(4)*: its presence in the ozonization product could be proved by NMR spectroscopy, but all attempts to isolate the compound, or even to store the ozonization product, afforded a polymeric material on the one hand, and the much more stable and nicely crystalline, but entirely useless all-*trans*-isomer *(6)* on the other. Under no conditions tried could formation of the desired Diels-Alder product be detected.

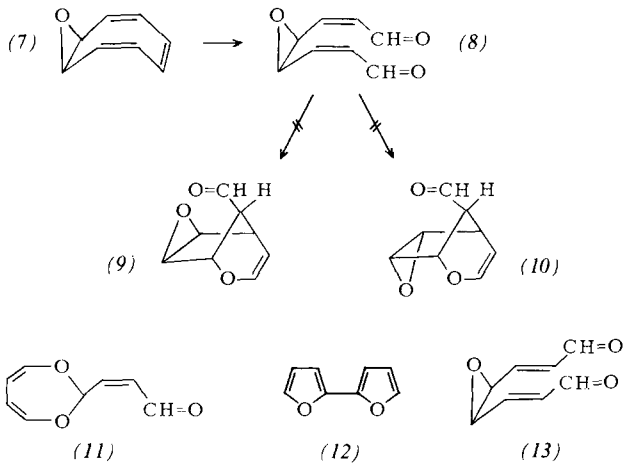
2.2. The Aldehyde *(9)* or *(10)* as Planned Precursor

The original idea, appealing as it was, did not work in the case of compound *(4)*. However, it was too attractive to be abandonded before all its potentialities had been exhausted. Since the instability of the all-*cis*-dialdehyde, obviously inherent in its high degree of unsaturation, seemed to be a major impeding factor, a correction of the initial plan was next suggested which should interrupt the conjugation while still maintaining the dialdehyde molecule in the all-*cis* configuration:

Cyclooctatetraene monoxide *(7)*, a known compound easily prepared from the hydrocarbon by peracid oxidation, should afford, on selective monoozonization, the all-*cis*-epoxydialdehyde *(8)*, hopefully more stable than the intermediate *(4)* first thought of. Besides interrupting the conjugation and keeping the molecule in the right configuration for the Diels-Alder

reaction, epoxidation would introduce the oxygen substituent missing in the original approach.

On the other hand, use of cyclooctatetraene oxide as starting material would incur additional risks: there were now two types of double bonds in the starting material and the ozonization could take place at the wrong site; the Diels-Alder reaction could *a priori* give two different products [*(9)* and *(10)*] of which only one might provide—by cleavage of the epoxide ring—the desired *cis* configuration of the two, 1,3-located, oxygenated functions.



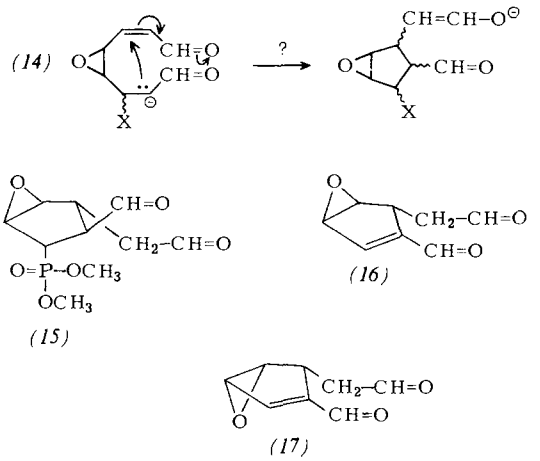
However, we were prepared to take the risks, especially since some of them no longer appeared that dangerous on thorough consideration. For instance, we could deduce that the most probable site of attack by ozone would be, as desired, the double bond most remote from the epoxide ring. This expectation proved to be correct and the new, crystalline all-*cis*-epoxydialdehyde *(8)* was the only defined product and could be isolated in satisfactory yields from the ozonization mixture.

As expected, the epoxy dialdehyde *(8)* was more stable than the conjugated all-*cis*-octatrienedial *(4)*. It could be chromatographed on silica gel and stored at low temperatures; on the other hand, it proved to be a very reactive compound with a special liking for surprising reactions. Thus, on heating at 100 °C in a hydrocarbon solvent, a rather unexpected electrocyclic reaction took place instead of the desired Diels-Alder cycloaddition and the interesting dioxacycloheptadiene derivative *(11)*—a combination of maleic and enolized succinic dialdehydes—was formed.

There were two more escape routes by which the dialdehyde avoided the planned Diels-Alder reaction (for which the orbital overlap in the spiral conformation was probably not very favorable): With acids and with some metal salts (mercuric sulfate), 2,2'-bifuryl *(12)* was formed. And with basic agents such as pyridine or triphenylphosphane, the *cis*-dialdehyde changed to the more stable *trans,trans*-isomer *(13)* (again useless for a direct Diels-Alder reaction).

2.3. The Aldehydes *(15)*, *(16)*, and *(17)* as Precursors

We felt that the *cis-trans* isomerization *(8)* → *(13)* deserved more consideration in spite of the disappointing result. A reversible Michael addition of the base (nucleophile) to the conjugated system of the α,β-unsaturated aldehyde was the most probable mechanism and this raised the question whether a carbanion of the type of *(14)* formed by addition of a suitable nucleophile to one of the unsaturated branches would not attack the other branch in a kind of Michael addition, thus forming a cyclopentane system. In other words: If the one-step Diels-Alder reaction could not be realized, could we not at least achieve a step-wise ring-closure leading to the same or a similar result?



For that purpose, a number of nucleophiles were tried under various conditions on both the *cis-(8)* and the *trans*-epoxy dialdehyde *(13)*. (The *trans* stereochemistry of the double bond should not be restrictive in a stepwise process and a *cis*-to-*trans* isomerization was to be expected anyway under the conditions proposed.)

The first cyclopentane formation was observed with the *cis*-dialdehyde and excess trimethyl phosphite (methylene chloride, room temperature): In a mechanistically not entirely transparent process, dimethyl 2-formyl-3-formylmethyl-4,5-epoxycyclopentanephosphonate of the probable stereochemistry shown in *(15)* was produced in variable yields (40—50 %). The structure of this compound was somewhat reminiscent of that of *(2a)*, but the epoxide ring and the acetaldehyde side chain were *trans* oriented, and the phosphonate group was by no means an ideal substitute for the oxygenated function planned for that position of our key intermediate: The C—P bond was too strong and resisted all attempts at substitution or elimination.

Therefore we were very pleased when on treatment (in tetrahydrofuran or methylene chloride) with alkali *p*-toluenesulfinates in suspension or in homogeneous (dimethylformamide) solutions, both the *cis-(8)* and the *trans*-epoxy dialdehyde *(13)* were transformed to the novel dialdehyde *(16)* (37—42%). Here the nucleophilic reagent was not incorporated into the molecule, and a double bond conjugated to an aldehyde group was ready for the introduction of the missing hydroxyl.

The spectroscopic evidence left some doubts whether *(16)* or *(17)* had been formed, but another finding soon helped to answer this question unequivocally: With piperidine and piperidinium acetate, both epoxy dialdehydes *(8)* and *(13)* gave a stereoisomer of the novel dialdehyde and on comparison of the spectral data of both isomers it became obvious that in the product of sulfinate-catalyzed cyclization the groups were *trans* oriented [*(16)*] and in that of piperidine-catalyzed reaction *cis* oriented [*(17)*].

When compared to the structure of the desired dihydroxy dialdehyde *(2a)*, the isomer *(17)* in particular looked like a promising advanced intermediate. It was only three steps away from cyclooctatetraene and the epoxide ring merely had to be transformed into a—properly placed—hydroxyl group and another oxygen function to be introduced to convert the compound into one of the previously discussed forms of the key intermediate *(2)*.

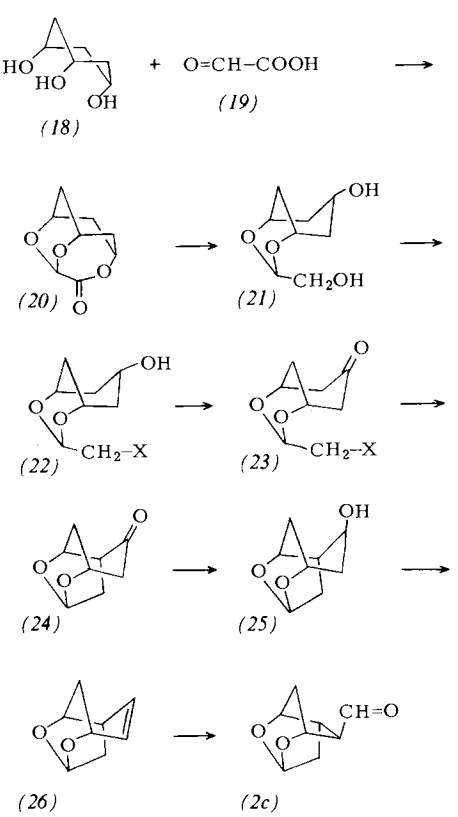
In the introduction to this paper, fairness and openness were pledged and the moment has now come to honor that promise. The good-looking scheme above does not tell much about problems of isolation and varying yields of rather unstable and hard-to-handle intermediates, and, as more and more information accumulated on the chemistry of the cyclic dialdehyde *(17)* the bigger grew the question marks between its formula and those of the desired final products.

At this time an entirely new approach to prostaglandin synthesis was designed as a potential alternative to the "cyclooctatetraene pathway". It soon became clear that this route showed great promise and all efforts were finally concentrated on this chance.

3. The Aldehyde *(2c)* as Planned Intermediate

3.1. Dioxaprotoadamantanone *(24)* as Planned Precursor

In the new approach, the basic concept of prostaglandin synthesis remained unchanged, *i.e.* the same C_8-dialdehyde unit was to be synthesized as key intermediate; however, among its previously discussed forms preference was now given to the tricyclic acetal aldehyde *(2c)*.



The starting materials were again simple and readily available: *cis*-1,3,5-cyclohexanetriol *(18)* (deliberately shown in its rather unusual axial conformation), easily prepared from phloroglucinol by Raney nickel hydrogenation, and the commercially available glyoxylic acid *(19)*. Why these two particular components?

Firstly, any two hydroxyl groups of the symmetrical triol have both the correct mutual 1,3-position *and* the *cis* configuration of the two ring hydroxyls in $PGF_{2\alpha}$ and, consequently, of the two acetal oxygens of the planned key intermediate *(2c)*. Two of the total of four chiral centers of the key intermediate were here "preformed" and the question of stereospecific introduction of the oxygenated substituents—as the reader may recall, a major problem in the cyclooctatetraene approach—was avoided by choosing this starting material.

Further, it was hoped that the six-membered ring of this component could later be contracted to a cyclopentane ring, the one carbon "in excess" becoming the aldehyde group of the key intermediate. For that purpose, the third hydroxyl group of the triol might be a welcome temporary functionality. Moreover, this third hydroxyl was to serve as an *ad interim* handle in the process of joining the triol with the other component.

The other component had to provide the two carbon atoms of the acetaldehyde side chain (protected in the key intermediate *(2c)* as a cyclic acetal). In glyoxylic acid, the aldehyde group was directly available and its notoriously high reactivity augured well for the planned reaction in which its mutual protection with two hydroxyls of the triol would be established. The carboxyl group, which should supply the other carbon of the acetaldehyde side chain, seemed to be, at the outset of the synthesis, an excellent counterpart to the hydroxyl "handle" in the joining process.

In other words, the plan was to combine, with the help of an acidic catalyst, cyclohexanetriol and glyoxylic acid to give the tricyclic acetal lactone *(20)*.

On subsequent reduction of the lactone grouping to the bicyclic, primary-secondary diol *(21)*, the other carbon atom originating from the glyoxylic acid would also reach the right oxidation level needed for the side chain, while the original aldehyde group would stay protected as an acetal.

Next, the side chain needed to be connected with the ring by a carbon-carbon bond. A conceivable way of achieving such a connection seemed to consist in transforming the primary hydroxyl of *(21)*, *e.g.* by a selective tosylation or mesylation, into a better leaving group [cf. *(22)*, $X = OSO_2R$] and oxidizing the secondary alcoholic group to a ketone. In the resulting, symmetrical ketone *(23)*, $X = OSO_2R$, the carbonyl would activate its α-positions for a base-induced intramolecular alkylation by the side chain sulfonate. (Here the reader will finally appreciate the help of the lactone "handle" in the first step of this sequence in securing the right stereochemical orientation of the side chain.)

In this way, dioxaprotoadamantanone *(24)* displaying many structural features in common with the tricyclic key intermediate *(2c)* should be formed. Only a ring contraction of a cyclohexanone to a cyclopentane carboxaldehyde would then be needed to complete the synthesis of the latter.

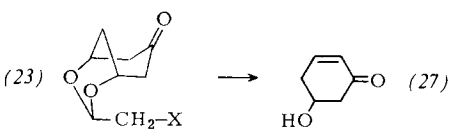
A number of methods were *a priori* available and there was no special preference for any one of them in the original plan, except that some restrictions were expected in connection with the general acid-lability of acetals (the same was true also for the preceding reactions). Of course, some possibilities were considered more often and as more promising than

others and our flow-sheet depicts, in rather general terms, such a "somewhat preferred" scheme: Reduction of the tricyclic ketone to dioxaprotoadamantanol *(25)*, a (probably two-step) elimination to the corresponding tricyclic olefin *(26)*, and, finally, a one- or multi-step ring-contraction of the latter to the cyclopentanecarbaldehyde derivative *(2c)*.

Let us now turn our attention to the first experimental results of this approach: an optimistic start and the first difficulties.

As expected, when cyclohexanetriol *(18)* and glyoxylic acid *(19)* were heated in a suitable solvent (*e.g.* glyme) in the presence of an acid catalyst (Amberlyst 15), a complicated multifunctional reaction process took place from which the nicely crystalline trioxahomoadamantanone *(20)* resulted as the only isolable product in a yield of more than 85 %.

The lactone grouping of this novel compound could be easily reduced by a number of agents, but best of all by sodium tetrahydridoborate in ethanol, in almost quantitative yield to the bicyclic primary-secondary diol *(21)*. In full agreement with the plan, the reactivity of the two hydroxyl groups in *(21)* proved to be sufficiently differentiated for a highly selective tosylation of the primary alcohol. The crystalline monotosylate *(22)*, X = OTs, resulting in good yield on treatment of the diol in pyridine (−20 °C) with slightly more than one equivalent of tosyl chloride, was next oxidized by chromium oxide-pyridine complex in methylene chloride to the, again nicely crystalline, bicyclic ketone *(23)*, X = OTs (92 % yield).

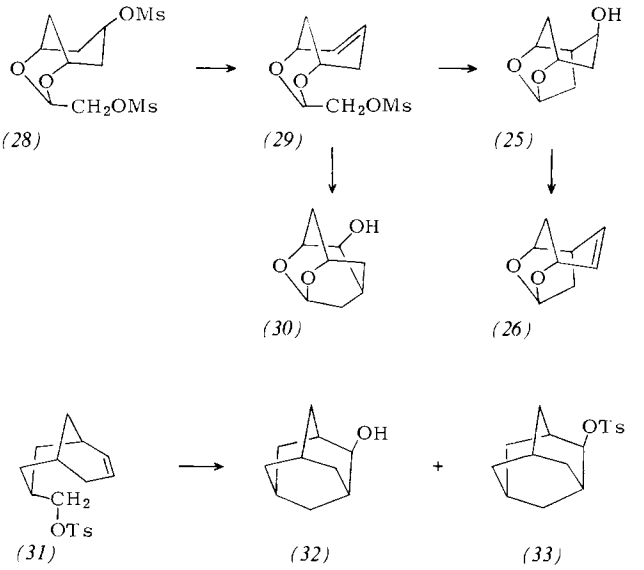


However, when the latter compound was treated with various basic agents (potassium *tert*-butoxide in *tert*-butanol or in glyme, 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) in benzene, solid sodium carbonate at 250 °C/0.5 torr, *etc.*) to initiate the desired intramolecular alkylation, a feared alternative reaction, namely elimination of the alkoxy-type substituent from the β-position, took place and, instead of the tricyclic ketone, a rather trivial cyclohexenone derivative *(27)* was obtained. Thus, the new plan badly needed correction.

3.2. The Olefin Mesylate *(29)* as Precursor

It seemed conceivable to transform the diol *(21)*—*via* a ditosylate or dimesylate *(28)*—into a bicyclic olefin monosulfonate *(29)* and to use the latter as substrate in a solvolytic reaction, in the hope that the π-electrons of the double bond would participate in the process and thus provide a carbon-carbon bond between the ring and the side chain. The literature supplied several examples of such a π-route to polycyclic systems, the closest one to our case being that described by *Raber*, *Kane*, and *Schleyer*[5]:

The unsaturated bicyclic tosylate *(31)*—a carbocyclic analog of the olefin-sulfonate *(29)*—when hydrolyzed in 80 % aqueous acetone at 25 °C afforded 95 % of 2-adamantanol *(32)*, along with 5 % of 2-adamantyl tosylate *(33)*, the reaction being 10^4 times faster than the solvolysis of the corresponding saturated compound under otherwise similar conditions.



Another, even more amazing manifestation of the propensity of the unsaturated compound *(31)* for cyclization was its spontaneous transformation into 2-adamantyl tosylate *(33)* in deuteriochloroform at 6 °C.

As already mentioned, the geometry of our olefin mesylate *(29)* would be very similar to that of the substrate *(31)* including even the right orientation of the side chain for a reaction with the double bond. Consequently π-participation in solvolysis was to be expected even here. However, an open question was what effect the two oxygen atoms would have both on the rate of solvolysis and which of the doubly bonded carbon atoms in *(29)* would become involved in the new carbon-carbon bond. The latter question was especially important for our plans.

Schleyer's case exemplifies the preference in carbocyclic chemistry for the unstrained adamantyl system; the exclusive formation of 2-adamantyl derivatives suggested that, whatever the steric and polar effects of the two oxygen atoms in our substrate might be, dioxaadamantol *(30)* would be an unstrained compound and hence warrant consideration as a possible solvolysis product of *(29)*.

Of course, this direction of bond formation would by no means be ideal for our purpose, since the side chain in the key intermediate *(2c)* should be connected to the carbon *next* to the oxygen-substituted ring member, but again, there were carbocyclic examples available of how to convert a 2-adamantyl derivative into protoadamantene, *i.e.* into a carbocyclic analog of the tricyclic olefin *(26)* of our synthetic scheme.

Moreover, we could expect that in our olefin mesylate *(29)* the inductive effect of the oxygen in the allylic position to the double bond might reverse the mode of addition observed in the carbocyclic system in the desired sense by concentrating the π-electrons at the closer carbon of the double bond and thus increasing its nucleophilicity. The same effect should also destabilize the otherwise stereochemically preferred 2-adamantyl carbonium ion and lead to the same result, *i.e.* formation of the dioxaprotoadamantyl alcohol *(25)*.

Let us once more turn our attention from the plan to experimental reality. This time the adjusted scheme worked perfectly: The bicyclic dimesylate *(28)*, the product of a high-yield reaction of the diol *(21)* with excess mesyl chloride in pyridine, when treated with basic agents under various

conditions, afforded the desired olefin mesylate *(29)* in invariably good yields.

Here a small practical note is timely: For the latter elimination reaction we tried a large variety of bases, the fancy ones such as DBU in dimethyl sulfoxide or tetrabutylammonium fluoride in dimethylformamide first, only to find later that potassium hydroxide in isopropanol did the job just as well and that five minutes' refluxing with this inexpensive reagent afforded *(29)* simply and in excellent yields.

The very first solvolysis of the olefin mesylate in boiling aqueous potassium carbonate—a simple experiment attended by much excitement—substantiated our expectations: it was gratifying to isolate the nicely crystalline dioxaprotoadamantanol *(25)* as by far the major product of the reaction. A thorough analysis later revealed about 5—8 % of the less desirable isomeric dioxaadamantanol *(30)* in the crude alcoholic product, thus showing that the difference in the energies of activation of the two competing ring closures was only small. However, the presence of the isomer *(30)* did not cause any practical complications; it could be easily removed in the course of the following steps.

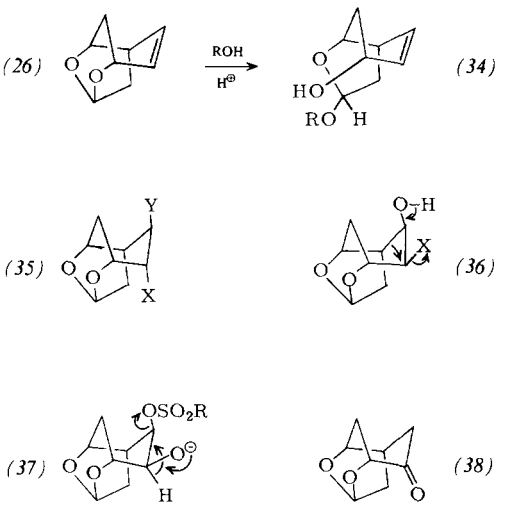
Dioxaprotoadamantanol *(25)* was the second chiral compound in our sequence—the first one was the olefin mesylate *(29)*—but it was the first one suitable for a resolution. For this purpose the racemic alcohol was converted into a diastereomeric mixture of esters of (+)-ketopinic acid, from which the less soluble (−)-diastereomer could be obtained pure on repeated crystallization from ethyl acetate in a yield of 78 %. The positive Cotton effect displayed by the corresponding ketone proved the levorotatory alcohol obtained from the ester diastereomer mentioned by alkaline hydrolysis to have the absolute configuration shown in *(25)*. It was the configuration needed for the synthesis of natural $PGF_{2\alpha}$. (From this point on, the synthesis was followed on two lines, both with racemic and with optically active materials.)

The tricyclic alcohol *(25)* was transformed in two simple operations—mesylation and elimination with KOH in isopropanol—into the corresponding olefin [dioxaprotoadamantene *(26)*] in an overall yield of 88 %. At this point, the reader will appreciate that the correction of the original scheme was not just an inconvenient emergency solution: It abbreviated the route to *(25)* by one step and the yields of all steps up to the olefinic compound *(26)* were excellent.

3.3. The Planned Ring Contraction of Dioxaprotoadamantene *(26)* to *(2c)*

The tricyclic olefin *(26)* was a chemically very interesting compound; however, not all of its reactions were desirable or useful for its final ring contraction to *(2c)*. Thus, the obviously strained cyclic acetal system of *(26)* proved to be extremely sensitive toward acids. Even trace amounts of aqueous or alcoholic acids opened the tricyclic system to form the corresponding bicyclic hydroxy hemiacetal *(34)*, R = H, and hydroxy acetals *(34)*, R = alkyl, respectively. With acids in the absence of any hydroxylic agent, insoluble polymeric material was immediately formed, obviously by a similar mechanism. This pronounced instability toward acids was certainly one of the reasons why a "direct" ring contraction of the tricyclic olefin *(26)* with thallium salts failed under various conditions.

A number of electrophilic agents such as bromine, bromonitrate, iodoazide, dichlorourethane, *etc.* added to the double bond of the dioxaprotoadamantene *(26)*, most of them in a both highly stereo- and regiospecific way, to give diaxial products of the common structure *(35)*.



The preference for diaxial products, although perfectly understandable, was by no means favorable for the planned ring contraction. As documented by many examples, a ring contraction of a 1,2-disubstituted cyclohexane can take place only when the leaving substituent is *equatorial* and thus antiperiplanar to the migrating C—C bond.

Only one addition reaction among those we tried afforded a promising adduct in this respect: Hydroxylation with osmium tetroxide giving the crystalline *cis*-diol *(36)*, X = OH, in an acceptable yield of about 55 %.

It could be expected that, on treatment with one equivalent of a sulfonyl chloride, only the equatorial hydroxyl of this diol would react to give a product *(36)*, $X = OSO_2R$, ideally suited for a ring-contracting elimination.

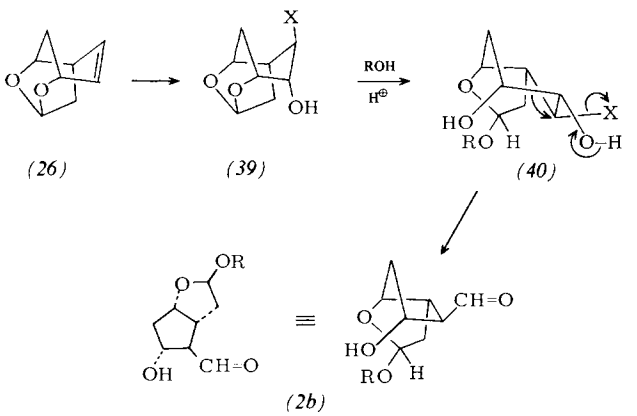
The first part of the plan was easy to implement: Even with an excess of brosyl chloride in pyridine, only the equatorial monobrosylate *(36)*, $X = OSO_2C_6H_4Br$, was formed in an excellent yield. However, when the compound was solvolyzed in boiling aqueous glyme in the presence of potassium carbonate, or on treatment with potassium *tert*-butoxide in *tert*-butanol, a rather unexpected product was obtained instead of the desired *(2c)*: the tricyclic cyclohexanone derivative *(38)*.

What could have happened here? The desired ring contraction, perfectly permissible from a stereochemical vantage point, would develop a temporary positive charge on the "brosylate carbon" and was thus obviously impeded by a destabilizing negative inductive effect of the neighboring acetal oxygen [an effect we have already met in the preferred formation of our dioxaprotoadamantanol *(25)*]. This probably opened the way for a less usual, but not entirely unknown reaction, *i.e.* a sulfonyl transfer from one oxygen to the other. In the isomeric brosylate *(37)* thus formed, the above-mentioned inductive effect was no longer operative and elimination of the sulfonate group with a hydride shift from an antiperiplanar position took place, resulting in the formation of the ketone *(38)*. It was also conceivable that an increase in the steric strain was another factor disfavoring a ring contraction.

If we summarize the accumulating experimental evidence at this point, the tricyclic olefin *(26)* would appear as a uniquely unsuitable intermediate: all its characteristic features—steric strain, destabilizing polar effects, acid-lability, preference for diaxial adducts—seemed to oppose our ring contraction plans.

4. The Aldehyde *(2b)* as Key Intermediate

If we did not want to give *(26)* up as an intermediate, it was necessary to change our approach to it. It occurred to us that the following scheme or one like it could provide a solution to this problem.

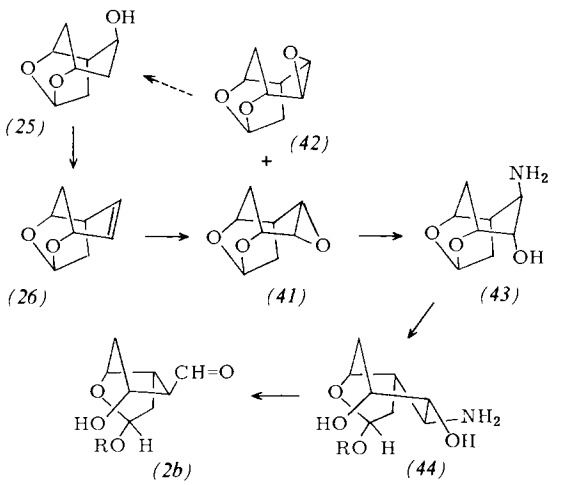


A diaxial adduct of the common formula *(39)* was needed in which X would be either a good leaving group or a function easily convertible into a good leaving group. It was obvious from molecular models and from experimental evidence on model compounds that, if we then opened the tricyclic system of such a derivative the cyclohexane ring, forced in the rigid original system of *(39)* into its boat conformation, would be able to assume the much more preferred chair form *(40)* with both substituents (X and OH) flipping into equatorial positions. Ring opening of this kind by acid-catalyzed alcoholysis has already been mentioned in Section 3.3 in connection with the tricyclic olefin *(26)*.

An elimination of X could then proceed with migration of the antiperiplanar carbon-carbon ring bond thus producing a cyclopentanecarbaldehyde with the aldehyde group in a *trans* position to the other three substituents. In other words: an excellent bicyclic key intermediate already considered previously [*(2b)*] would be formed. In this way, the hitherto hostile properties of the tricyclic olefin *(26)*, *i.e.* formation of diaxial adducts, easy acid-catalyzed cleavage, and the trend to diminish rather than to increase the ring strain, would all be used to our advantage. The following paragraphs will show how this idea was transformed into reality.

When treated at room temperature with a methanolic solution of benzonitrile and hydrogen peroxide in the presence of solid potassium hydrogen carbonate[6] the tricyclic olefin *(26)* was converted into a mixture of two crystalline stereoisomeric epoxides in which the desired *endo* isomer *(41)* was the major component. Since the *exo*-epoxide *(42)* could be easily separated by alumina column chromatography and returned to the synthetic scheme by lithium tetrahydridoaluminate reduction to the tricyclic alcohol *(25)*, its formation did not involve any appreciable loss of material. It is interesting to note that with *m*-chloroperbenzoic acid in methylene chloride or in chloroform, the ratio of both epoxides was reversed and mainly the unwanted *exo* isomer *(42)* was formed.

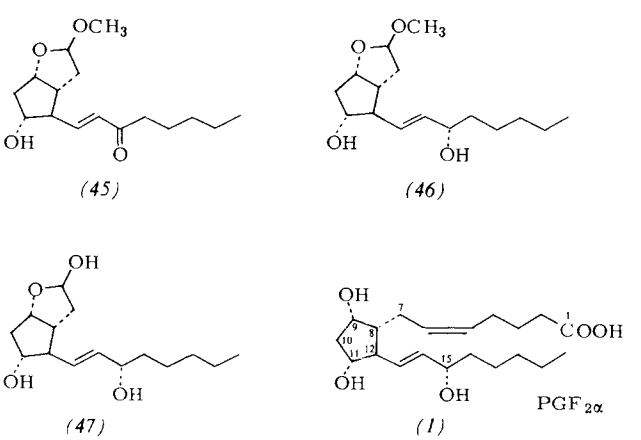
The *endo*-epoxide *(41)* was next heated at 100°C for 2h with concentrated aqueous ammonia. As a consequence of



the rigid conformation of the substrate, the epoxide ring was opened regiospecifically and a single product, the crystalline diaxial amino alcohol *(43)* was isolated in a yield of more than 90%.

When a solution of *(43)* in an excess of methanolic hydrogen chloride was stirred at room temperature, a crystalline hydrochloride soon started to precipitate and was finally obtained in quantitative yield. Its elemental analysis and spectral behavior were in full agreement with the structure of the bicyclic amino diol acetal *(44)*, $R=CH_3$. A large increase in the value of the vicinal coupling constant between the hydrogens on the two carbons bearing the OH and NH_2 groups [from $J\approx 0$ in *(43)* to $J=11$ Hz in *(44)*] was convincing proof for the expected conformational change, the original equatorial position of these two hydrogens having become axial.

As a pleasant consequence of this conformational change, the next step took the expected course: Diazotization of the hydrochloride of *(44)* dissolved in dilute aqueous acetic acid (containing some sodium acetate) with an excess of sodium nitrite afforded the desired key intermediate *(2b)* in yields of 80—85%. Unfortunately, if by no means surprisingly, this crucial intermediate of our prostaglandin synthesis was the only noncrystalline compound of the whole sequence to this



point and, as a rather unstable β-hydroxy aldehyde, unsuitable for further purification. However, both its spectral and its chemical behaviour unequivocally confirmed its structure.

The acetal aldehyde *(2b)* fulfilled our expectations as a useful intermediate for the prostaglandin synthesis. Thus, when it was heated at 60 °C in glyme with 1-(triphenyl- or 1-(tributylphosphoranylidene)-2-heptanone, a crystalline unsaturated ketone was formed in yields of 75—79 %; elemental analysis as well as all spectral evidence pointed to the structure *(45)*. The ketone was reduced with zinc tetrahydridoborate to an approximately equimolar mixture of the diol *(46)* and its 15β-epimer. Both isomers were separated by column chromatography and the unwanted β-epimer recycled by manganese dioxide oxidation to the enone *(45)*.

Both epimeric diols were characterized by spectral data and by nicely crystalline and well analyzing bis-*p*-nitrobenzoates. The racemic diols had been prepared by an entirely different sequence in 1970 by *Corey* and *Noyori*[7] and the 15α-epimer *(46)* converted into DL-$PGF_{2\alpha}$.

Adopting the procedure of these authors for the last two steps we first hydrolyzed the acetal function of *(46)* to the corresponding hemiacetal *(47)* using a dilute hydrogen chloride solution in aqueous acetonitrile (or glyme). And. when the crude hemiacetal was treated at 50 °C with an excess of ω-(triphenylphosphoranylidene)pentanoate in dimethyl sulfoxide. racemic or. in case of the optically active starting material, dextrorotatory prostaglandin $F_{2\alpha}$ *(1)* were obtained in yields of about 80 %. Both the spectral and chromatographic behavior of our synthetic products as well as the optical rotation of the dextrorotatory compound were in agreement with the published data for DL and natural $PGF_{2\alpha}$.

Thus, after somewhat less than a year of concentrated effort, the desired objective of the synthesis of prostaglandins was successfully achieved. As the present report shows, the way was not always straight and smooth. However, the proper choice of the key intermediate, the flexibility inherent in the synthetic conception, and the consequential and creative adaptation of the plans to new, experimental experience made the final solution of the synthesis possible without sacrificing any of its aspired features: high stereospecifity, low number of synthetic steps, avoidance of special protecting operations, simple and easily accessible starting materials, simple reagents, simple, efficient and easy-to-perform reactions.

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Chemical Ecology— A Chapter of Modern Natural Products Chemistry[**]

By Hermann Schildknecht[*]

The chemical reaction of arthropods to their environment, *i.e.* their chemical ecology, can be studied particularly well with water beetles. *Stenus comma*, an aquatic beetle weighing only 2.5 mg, saves itself from drowning with the aid of an alkaloid, and the water beetle *Ilybius fenestratus* defends itself against small mammalian predators with a compound belonging to the same class. The water beetle *Platambus maculatus* employs a diterpene for precisely the same purpose and the whirligig beetle a norsesquiterpene, which also offers protection against troublesome microorganisms. As chemical artists, the ants can hardly be surpassed. In particular, the myrmecine ants guarantee their food supplies with plant growth substances. Since these compounds, depending upon concentration, can also act as inhibitors, we are confronted with an excellent example of an ecological equilibrium being established with the aid of organic chemicals. Even the little parasitic bombardier beetle *Paussus favieri* is tolerated, on account of its defensive chemistry, in the nest of the myrmecine ant *Pheidole*. In contrast, inorganic compounds are largely responsible for the stability of spiders' webs.

1. Introduction

The ability of living creatures to adjust to the world in which they live, to shape and maintain their *Lebensraum* and to propagate therein is a consequence of aeons of development, during the course of which all organisms have come to terms with reality[1].

The result is an optimal adaptation of fungi, plants, and animals to their environment—both on the level of cellular development and on the level of morphogenesis—which is characterized by pronounced interaction between the individual species and its environment. The entire field of science concerned with the relations of an organism to its surrounding

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external world, to the organic and inorganic conditions of its existence, was designated ecology by *E. Haeckel* over a century ago[2]. As in all areas of life, chemically defined substances will play a role here—if they are known then we are justified in speaking about "chemical ecology". Chemical ecology attempts to interpret biological phenomena in terms of chemical compounds, and to answer the question "wherefore?". However, this only became feasible with the advent of methods for isolating, purifying, and analyzing minute quantities of natural products, *i.e.* methods permitting comprehensive analysis.

One of the most interesting and instructive biotic communities is the biocenosis in and around bodies of water, *i.e.* where life most probably originated and developed. In the course of millions of years, just as elsewhere in the biosphere, an equilibrium state was reached with regulatory processes which protect the way of life of, *e.g.* insects against interfering effects of widely differing kinds. Thus water is directly and indirectly an essential component of the biotope of animals living on the banks of stagnant or flowing water; however, it becomes highly dangerous if they cannot swim.

2. Chemical Ecology of *Stenus comma*

While hunting for springtail on the banks, the strangely blue-green colored staphylinid *Stenus comma*, measuring some 5 mm (Fig. 1), sometimes loses its grip in a light breath of

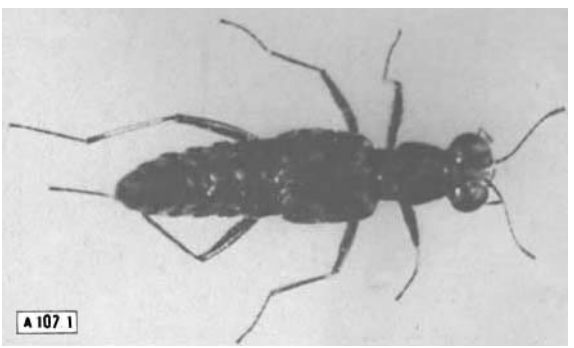
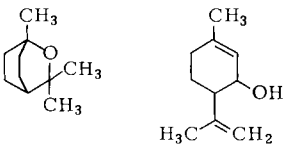
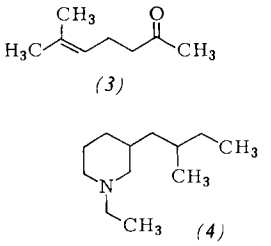


Fig. 1. *Stenus comma*.

wind—after all it only weighs 2.5 mg—and falls into the water. With a great effort it can keep itself above water by crawling and would reach the bank with great difficulty—or not at all if it were caught in a current and driven further away from land—if it were not able to move over the surface of the water without using its legs[3]. After briefly dipping the tip of its abdomen into the water it can dash over the surface at 40 to 75 cm/s, using its mobile abdomen as a rudder; like a water skier it does not sink at that speed.

More than 70 years ago, *Billard* and *Bruyant*[4] *recognized* that beetles of the genus *Stenus* are propelled forwards by a substance released from their anal end onto the surface of the water and compared its action with that of camphor or thymol. Indeed, the beetle secretion extracted from water with ether has an odor resembling that of eucalyptus oil, while also being amine-like. In order to perform detailed analyses we distilled the abdomens of 1000 beetles, extracted the distillate with benzene, concentrated the solution by ice zone melting, and separated it into five fractions by gas chromatography[5]. The substance present in the second most important fraction (0.8 mg) was found by mass spectrometry to have a molecular formula $C_{10}H_{18}O$ and was identified primarily by ^{1}H-NMR spectroscopy as 1,8-cineole *(1)* (eucalyptol); the substances occurring in two other less important fractions were identified as an isomer of isopiperitenol *(2)* and as 6-methyl-5-hepten-2-one *(3)* by comparison of IR spectra.



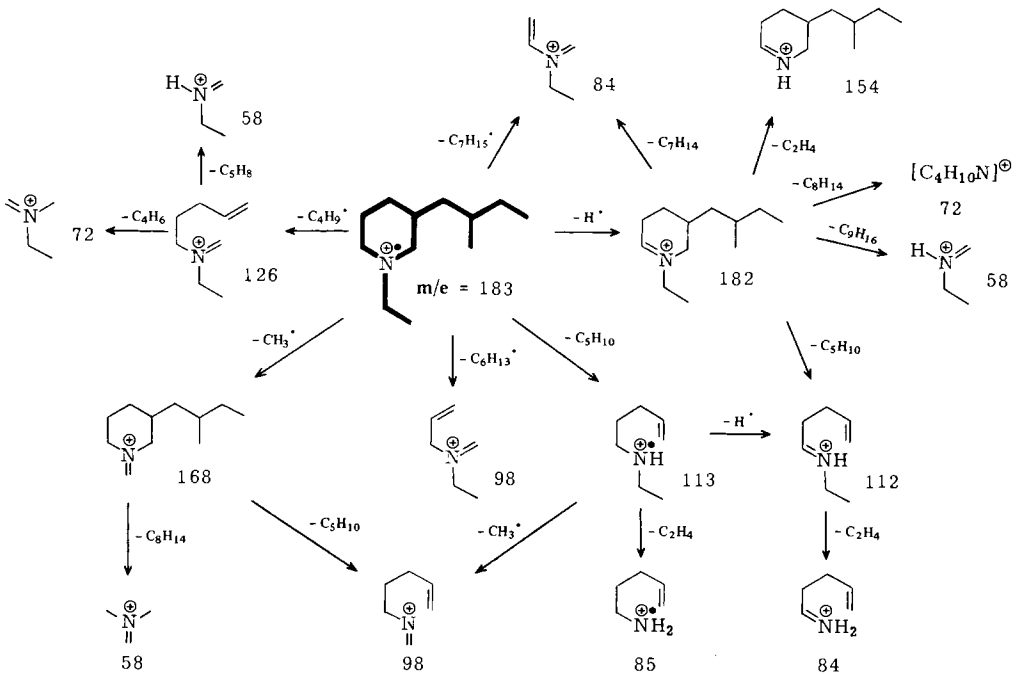


This substance alone would explain the propelling action of the secretion because eucalyptol spreads well on water. However, apart from the little pygidial defensive bladder in which it stores compounds *(1)*—*(3)*, *Stenus comma* also possesses a larger bladder from which two fractions having an unpleasant amine-type odor are obtained on workup as described above. The substance present in the principal fraction, 6 mg from 1000 beetles, was called stenusin; it is an oily compound having the molecular formula $C_{12}H_{25}N$. All structures deduced mainly from ^{1}H-NMR data were shown, by comprehensive spectral comparison of synthetic piperidine and perhydroazepine derivatives with the natural product, to be incorrect[6]. This provided a particularly clear demonstration that even the slightest deviation in absorption spectra of comparison substances must be given serious consideration in the structural elucidation of an unknown natural compound. We finally concluded, contrary to the predictions based on ^{1}H-NMR spectra, from a detailed mass-spectrometric analysis that the doubly substituted piperidine derivative *(4)* must be present. The fragmentation scheme affording structural proof is based, *inter alia*, on measurements of metastable transitions[7].

Stenusin *(4)* constitutes 80 % of the pygidial gland secretion of *Stenus comma* and purely on that basis is the actual propellant. Confirmatory evidence comes from the physical data[*]. As expected for a substance which spreads on water, stenusin is only very sparingly soluble in water (0.03 wt.-%) and therefore lowers the surface tension only slightly, from 72.8 to 49 dyn/cm[*]. This is reason enough for not speaking of "relaxation" swimming, although this term is frequently encountered in the literature[8], because stenusin *(4)* does not lower the surface tension of water to 25—30 dyn/cm like normal surfactants. Instead, the high spreading pressure of $p = 28.46$ dyn/cm is responsible for the motion of the beetle.

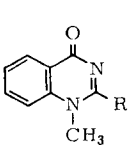
As already hinted, *Stenus comma* possesses two pairs[9] of abdominal bladders filled with chemicals, which most probably originated as defensive organs. This conclusion is supported by chemical aspects, since the contents of such pygidial defensive glands will have formerly prevented attack by microorganisms as in the case of land beetles[10]; a suitable compound is 1,8-cineole *(1)* which is known as an antiseptic. We may

[*] We are grateful to Dr. *Pohlemann*, BASF AG, for determining the physical data of stenusin.

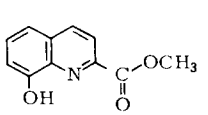


assume that in the course of evolution the chances of survival proved to be greater as the beetle is not only resistant to microorganisms but can also move rapidly on water. A suitable compound favoring development of this mode of swimming was eucalyptol *(1)* having a surface tension of $\sigma = 28.5$ dyn/cm; however, owing to its relatively high solubility of 0.3 % its spreading pressure is only $p = 2.16$ dyn/cm. Perhaps by chance, oxygen was replaced by nitrogen in the biogenesis of the terpenoids of the small pygidial defensive glands: the result was the diterpenoid stenusin *(4)* having a low solubility in water and hence an extremely high spreading rate of 32.5 cm/s, yet maintaining sufficient solubility to avoid permanent "contamination" of the surface. Moreover, stenusin renders the body of the beetle strongly hydrophilic and thus reduces drag by as much as 30 %. The little staphylinid *Stenus comma* therefore skates over the water, rather than swimming, on releasing its propellant.

Stenusin is the third alkaloid we have found as defensive substances in arthropods. Glomerine, from the segmental glands of the millipede *Glomeris marginata*, was identified as 1,2-dimethyl-4-quinazolone *(5) inter alia* by electron pyrolysis[11]; in addition, the sticky colorless and odorless toxic secretion is found to contain the homologous 2-ethyl-1-methyl-4-quinazolone *(6)*. Methyl 8-hydroquinolinecarboxylate *(7)* is the predominant toxin in the prothoracic defensive secretion of *Ilybius fenestratus*[12] which leads an amphibious existence and has therefore developed toxins active against cold-blooded predators in and around the water and also against small mammals living on land. The toxin active against mammals is the alkaloid *(7)*, while steroids[10] are used in defense



(5), R = CH_3
(6), R = C_2H_5



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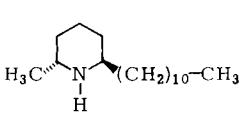


(8)

against predatory fish. The alkaloid colors the secretion yellow; thus the blackish-brown water beetle displays the animal warning colors yellow/black only when in acute danger, *e.g.* when taken between thumb and index finger it presses two large drops of poison from two slits at the front edge of the prothorax.

All three alkaloids *(4)*, *(5)*, and *(7)* exhibit the same effect when administered to mice: they produce clonic spasms. In the absence of comparative experiments, it cannot yet be said whether stenusin *(4)* is also used as a defensive substance against insectivores, as established so far only for glomerine *(5)* and for the alkaloid *(7)* from *I. fenestratus*. In this context, it is interesting to note that the defensive alkaloid of the fire ant *Solenopsis saevissima*, solenopsin A *(8)*, is also a piperidine derivative[13].

3. The Defensive Chemistry of *Platambus maculatus*

Just as *Stenus comma* have developed a terpenoid and an alkaloid as defensive substances in the course of their evolution, the water beetles of the Colymbetinae subfamily also seem to have evolved along similar lines, except that in the latter case the two classes of compounds appear in two different species. As mentioned in Section 2, the substance accompanying the steroids in *Ilybius* is an alkaloid. In another species of the Colymbetinae, namely *Platambus maculatus* we expectly found a steroid, accompanied not by an alkaloid but by a crystallizing sesquiterpene[14].

Pl. maculatus, a water beetle measuring 7–8 mm and bearing a characteristic yellow marking on its black elytra, is found in the sluggishly flowing side-arms of the Isar river between aquatic plants or under pebbles. Its prothorax is partly transparent, permitting recognition of its prothoracic defensive bladders, filled with milky defensive secretion, as if through an inspection window glazed with yellow chitin (Fig. 2). The beetle visibly empties these bladders if stimulated on the head and the secretion can be drawn into fine glass capillaries and collected in methanol.

From 1000 bettles we first obtained 1 mg of the steroid *(9)*, melting at 232—234 °C. By thin-layer chromatography we also isolated 10 µg per beetle of a defensive substance *(15)*, melting at 63 °C, which we called platambin. Its structure was elucidated by modern physical methods and by micropre-

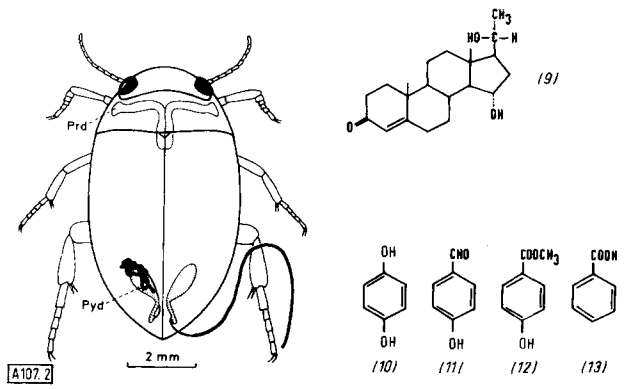
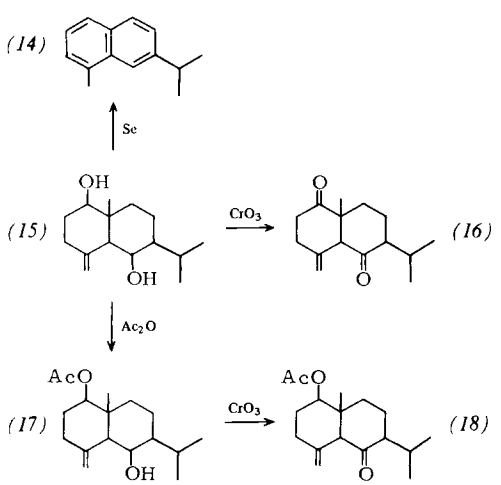
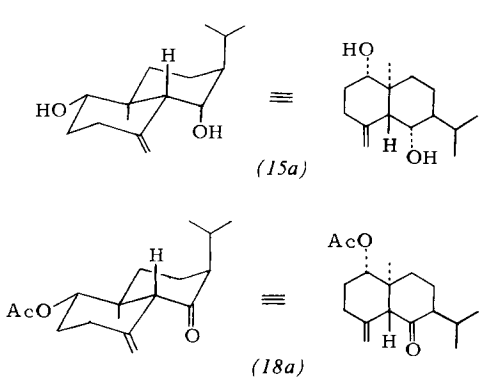


Fig. 2. The fast swimmer *Pl. maculatus* and its defensive substances *(9)* to *(13)*. Prd = prothoracic defensive glands, Pyd = pygidial defensive glands.

parative techniques. The molecular formula was established as $C_{15}H_{26}O_2$ by mass spectrometry. In keeping with the double bond rule we deduced a bicyclic system, which was substantiated by dehydrogenation with selenium to give eudalin *(14)*.



This indication of a sesquiterpene structure was supplemented by ^{1}H-NMR spectroscopy, which revealed the platambin molecule [*(15)*] to contain two secondary hydroxyl groups, an angular methyl group, an isopropyl group, and an



exocyclic double bond. The relative position of the double bond could also be deduced from the shift of the methyl proton signal after partial acetylation to *(17)* and oxidation of the hydroxyl group to give *(18)*; finally the complete constitution of platambin followed from a mass spectrum of *(16)* with a base peak at 123. Each half-molecule obtained on fragmentation accordingly contains only one carbonyl group.

The stereochemistry of platambin was determined by measurement of circular dichroism, which showed natural platambin to be the enantiomer 7α*H*,5β,10α-eudesm-4(14)-ene-1α,6α-diol *(15a)* (Fig. 3).

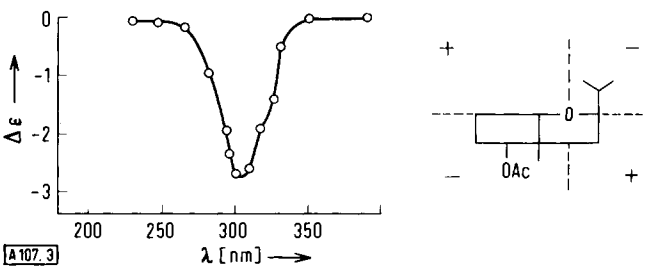


Fig. 3. Circular dichroism of the 1-acetoxy-6-ketone *(18a)* obtained from natural platambin (with octant projection).

We do not yet know anything about the physiological properties of platambin *(15)* since adequate amounts for a screening test only became available once it had been synthesized. However, we may justifiably expect that platambin is also an effective defensive substance against small mammals—such as shrews—since *Pl. maculatus* protects itself against attack by poikilothermal vertebrates with the steroid fraction of its prothoracic defensive secretion. Like all other beetles of the Dytiscidae family, *Pl. maculatus* is armed against attack by bacteria, fungi, and Campanularia with phenolic compounds, which it stores in high concentration in its pygidial defensive bladders. This antiseptic gland system produces mainly *p*-hydroxybenzaldehyde *(11)*, benzoic acid *(13)*, and methyl *p*-hydroxybenzoate *(12)*, which has never yet been absent in any of the water beetles we have studied, and finally also hydroquinone *(10)*.

Let us now consider the chemistry of a water beetle which possesses only pygidial glands.

4. Chemical Ecology of Whirligig Beetles

On ponds and in places where a stream or river flows only sluggishly, and then mainly under bridges, the lustrous whirligig beetle *Gyrinus natator* (Fig. 4) can be seen carelessly tracing circles, loops, and spirals; up to one hundred of these gregarious little beetles are frequently observed in one place.

However, the Gyrinidae can also be highly nervous. The slightest cause for disquiet suffices to send them over the surface of the water at a speed of up to 1 m/s; and if they still feel threatened during their flight they will suddenly dive. Of the many water beetles we have so far observed, the whirligig beetles number among those which have adapted extremely well to their environment. Their bodies resemble boats in shape, their legs serve as oars for a highly refined swimming technique, and, according to *Nachtigall*, *Gyrinus* possess the best apparatus for forward motion yet to be found in the

animal kingdom[15]. When fleeing from predators, the beetle can follow a zig-zag course like a hare on land; the rowing frequency of its hind legs can reach 50 to 60 strokes per second. In spite of its high speed the beetle does not collide with solid obstacles since it locates them by means of V-shaped capillary waves which it utilizes after the manner of an echo-sounding device[16, 17]. Thus the whirligig beetle can be regarded as the counterpart of the bat in an aquatic environment.

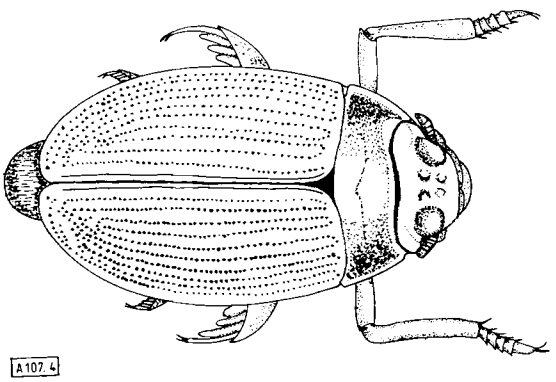


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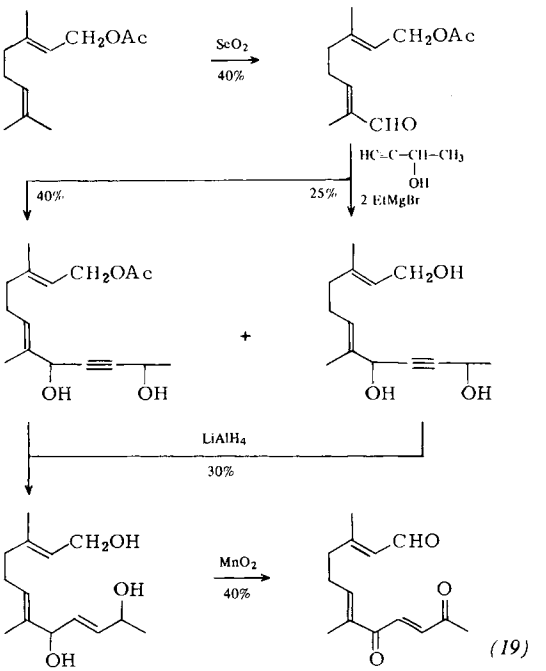
Fig. 4. *Gyrinus natator.*

It would come as a surprise if this fantastically constructed "physical ecology" were not complemented by a highly advanced "chemical ecology", or if the former did not actually owe its existence to the latter. However, this would mean that the whirligig beetle possesses organs producing and secreting the necessary substances. Such organs are the pygidial defensive glands which had hardly been examined until a few years ago. They could be ascribed the same antiseptic function as the pygidial defensive bladders of the Dytiscidae; such a conclusion is justified by the cleaning ritual of the Gyrinidae. Like many other species of water beetles, the whirligig beetles soon climb up on to pieces of floating cork in an aquarium. After waiting until they have dried, the beetles then vigorously move their abdomen up and down and finally brush with their rear legs over the edge of their downward-arched abdomen, their belly, and sometimes under their elytra, most probably distributing the secretion of the pygidial defensive glands. This secretion is toxic to microorganisms living on the surface of water such as bacteria, flagellates, algae, amoebae, and ciliates[18]. Any of these organisms which may have attacked the elytra of the whirligig beetle are killed within minutes by the action of the secretion. In this connection, we were particularly interested to know whether the Gyrinidae use the same compounds for their bodily hygiene as the Dytiscidae, particularly since the Gyrinidae form a family of their own among the beetles.

The decomposable major component of the secretion, gyrinal, can be obtained under mild conditions by rapid high-pressure liquid chromatography[19] and crystallizes at 0 °C. Even the first preliminary experiments on gyrinal revealed the presence of an α,β-unsaturated keto aldehyde instead of a phenolic substance (cf. Fig. 2). A relative molecular mass of 234 (molecular formula $C_{14}H_{18}O_3$) was determined with a double focusing mass spectrometer; a 220-MHz ^{1}H-NMR spectrum confirmed the constitution of a norsesquiterpene bearing an acetyl group at the end of its chain. The positions of the two other double bonds and finally also that of the third carbonyl group followed from ^{1}H-NMR double resonance analysis[20]. The *trans* substitution of all three double bonds could only be confirmed by synthesis of gyrinal *(19)* from geranyl acetate which was performed independently in three laboratories[21–23].



(19)

The availability of synthetic gyrinal *(19)* allowed us to answer the remaining questions connected with the "whys and wherefores" of this sesquiterpenoid aldehyde. Tests with mice[*] showed gyrinal to be relatively toxic (DL_{50} *ca.* 45 mg/kg mouse); this means that every other mouse that has eaten ten beetles has to die because the pygidial defensive bladders, weighing about 200 µg, contain 80 µg of gyrinal. A critical examination of the defensive behavior of a typical aquatic species such as the whirligig beetle must of course also take account of predatory fish. Although the beetle can recognize its enemies in water just as quickly as above, possessing divided eyes, its underwater swimming speed is only about one-tenth of that on the surface.

Indeed, gyrinal is also toxic to fish[18]. This can readily be demonstrated with a small crucian carp (*Carassius carassius* L.) which is placed together with the contents of 20 pairs of glands in a beaker containing 140 ml of water; that corresponds to a gyrinal concentration of 10 mg/l. Initial disturbance of equilibrium gives way to a state of excitement, and the fish finally dies in a narcotic state after about an hour.

Thus gyrinal can be used as a defensive compound against both microorganisms and higher animals. This is supported by the following observation: whirligig beetles captured in spring after a long winter's rest nearly always have empty pygidial defensive bladders—perhaps because the beetles can only defend themselves against microorganisms by chemical means and hardly by mechanical measures—and that *Gyrinus*, like all other beetles equipped with defensive glands, possesses a characteristic "marking" for its enemies: a distinctive odor[24]. The odiferous substances are likewise located in

[*] We are indebted to Prof. *Lenke*, BASF AG, for the pharmacological screening.

the pygidial bladders and could be identified as isovaleraldehyde and isopentanol by coupled GC-MS analysis[25].

It remains to be established whether *G. natator* can more readily remain above water with the aid of the highly-surface-active compound gyrinal—they displace only half their total weight of water when floating on the surface[16]. In that case, gyrinal and the entire pygidial defensive gland secretion would have several functions and the whirligig beetles would be excellently established by virtue of their chemical ecology in the oldest biocenosis of living nature, that of the water. We see here an evolutionary peak, similar to that of the bombardier beetle, which is matched only by organisms whose development goes back further than that of the land beetles, namely ants.

5. Chemical Ecology of Myrmecine Ants

Apart from man, the only other animals founding highly organized colonies are the ants, the termites, and the bees. One can even speak of a cultural development in the case of the myrmecine ants. This subfamily contains tribes which reap and yet do not sow. These seed-gatherers are called harvester ants. A higher stage of development has been reached by the leaf-cutting ants, which have secured independence from a relatively uncertain food supply. They grow fungi on a mash of leaves and petals and sometimes even on refuse; only the hyphae of the fungi are taken as food for the ants and their brood. This "invention", dating back millions of years, has since been twice duplicated, namely by the macrotermitic termites and by a wood-boring beetle. According to *Martin*[26] this fungus-ant symbiosis has arisen *via* a complementary carbon-nitrogen metabolism of the participating organisms; however, in 1947 *Weber*[27] suspected a special

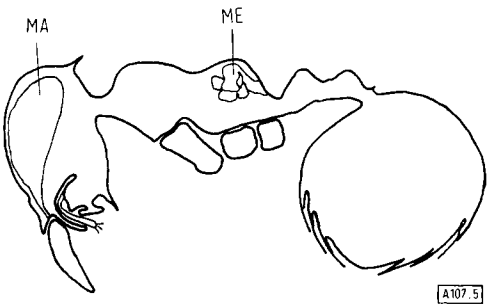
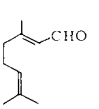
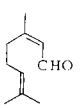
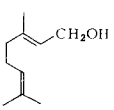
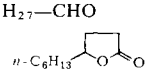
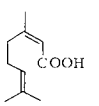
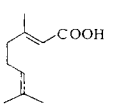
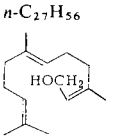


Fig. 5. Median vertical section of a small *Atta* worker; MA = mandibular gland, ME = metathoracic gland (from ref. [28]).

Table 1. Substances found in the mandibular glands of the leaf-cutting ant *Atta sexdens rubropilosa* Forel.

Cpd.	Method [a]	Content [µg/head]
β-Pinene	GC-MS	
CH_3—$(CH_2)_2$—$CH(CH_3)$—CO—C_2H_5 *(20)*	MS	0.4
CH_3—$C(CH_3)$=CH—$(CH_2)_2$—CO—CH_3 *(3)*	MS	0.09
n-C_8H_{17}—CHO	MS	0.08
n-C_9H_{19}—COOH	IR, MS	
n-$C_{10}H_{19}$—CHO	IR, MS	0.8
 Geranial *(21)*	*(21)*: IR, MS	20
 Neral *(22)*	*(22)*: IR, MS	21
Citral		
 Geraniol	IR, MS	0.2
C_6H_5—CH_2—CH_2OH	GC-MS	
n-$C_{12}H_{25}OH$	IR, MS	0.4
n-$C_{13}H_{27}$—CHO	IR, MS	0.5
	IR, MS	0.3
 Neric acid	IR, MS	
 Geranic acid		
n-$C_{25}H_{52}$	GC-MS	
n-$C_{27}H_{56}$	GC-MS	
 Farnesol	IR, MS	

[a] Identified by: GC-MS, combined gas chromatography/mass spectrometry; MS, mass spectrometry; IR, infrared spectroscopy.

substance to be present in the ant secretions—a very reasonable hypothesis in view of the role played by the diverse glandular secretions especially in the chemical ecology of the colony-forming insects. The leaf-cutting ants possess mandibular and metathoracic glands (Fig. 5).

In 1959, *Butenandt et al.* found geranial *(21)* and neral *(22)* in the mandibular glands[29]. Since we maintain our own *Atta* colony in the laboratory[*], we were able to considerably extend *Butenandt*'s analytical results by working with 20000 freshly prepared ants' heads. So far we have found 16 further constituents (Table 1)[30], which were isolated by gas chromatography and identified mainly by mass spectrometry. Among them, citral [*(21)* + *(22)*] has been identified as an alarm pheromone of *A. sexdens*. The same effect was observed for 4-methyl-3-heptanone *(2)* and, to a lesser extent, with 6-methyl-5-hepten-2-one *(3)*, in accord with the findings of *Riley et al.*[31]. Some time will certainly elapse until the entire substance complement of the mandibular glands has been elucidated. Little progress can be expected, however, without thorough behavioral studies.

The metathoracic glands are organs occurring pairwise on the metapleura, whose secretion is distributed to the environment. Our studies on the composition and function of the secretion were directed by the idea that the metathoracic glands might be the organs responsible for controlling the fungus garden. This assumption was also supported by our observation that, in contrast to the larger soldiers, precisely the small animals of the worker caste—responsible for tending the fungus garden—have the best developed glands, always copiously filled with secretion.

The first component of the secretion which we isolated by thin-layer/gas chromatography was identified by UV, IR, and mass spectra as phenylacetic acid *(23)*. In addition, we could also detect a more readily decomposable carboxylic acid by thin-layer chromatography; it was isolated by column chromatography of the metathorax extract from 40 ants on Sephadex LH 20. Of several comparison samples, only 3-indolylacetic acid *(24)* gave the same R_f value, the color reaction with van Urk reagent, and the same UV absorption as the component isolated by gel chromatography. After esterification of the secretion we could identify the corresponding fraction isolated on a Sephadex column as the methyl ester of *(24)* by mass spectrometry[32].

Heteroauxin *(24)* is one of the most widely distributed plant growth substances and we thus had the first significant evidence confirming our assumption that the metathoracic gland secretion is involved in cultivation of the fungi. Phenylacetic acid *(23)* also fits in with this concept because it functions as a growth regulator, either alone or even more effectively in combination with the acid *(24)*[33]. It has long been known that plant growth substances play a role in the chemical ecology of insects. In 1965 *Kaldewey*[34] reported that the larva of the gall wasp *Cynips querusfolii* L. transforms a growth substance precursor, most likely tryptophan, into a growth substance which is probably *(24)* according to paper chromatography. And *Calam*[35] has unequivocally identified the acid *(24)* in the salivary glands of the gall gnats *Dasyneura urtucae* and *D. affinis*.

At that stage we had isolated the two growth-regulating carboxylic acids *(23)* and *(24)* but not identified the major

[*] We are grateful to BASF AG for providing this colony.

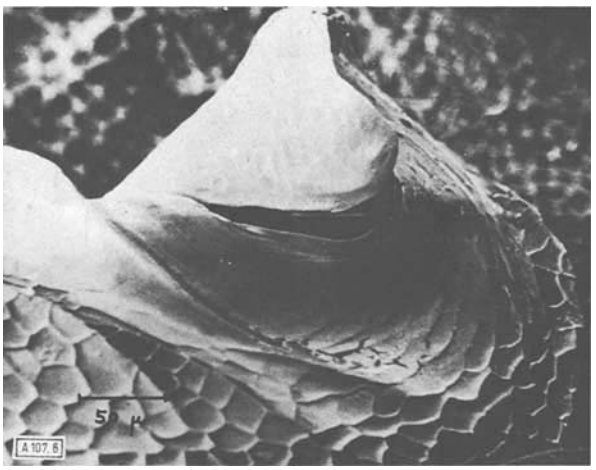


Fig. 6. Metathoracic gland of *Atta sexdens rubropilosa* Forel. Recorded with a scanning electron microscope (JSM-S1, Kontron GmbH).

component. On thin-layer chromatography of the secretion drawn out of the metapleural sacs (Fig. 6) this component could only be rendered visible with concentrated sulfuric acid; however, on isolation, again as the methyl ester, it gives an interpretable mass spectrum. Accordingly, having a molecular formula of $C_{10}H_{20}O_3$ and showing the base peak $m/e = 103$ typical of methyl 3-hydroxycarboxylates, it must be 3-hydroxydecanoic acid *(25)*[36]. The natural compound, myrmicacin, is the levorotatory D-acid having $[\alpha]_D^{20} = -3°$ (in $CHCl_3$) (see Table 2).

Table 2. Concentration ranges of the acids from the the metathoracic gland of the leaf-cutting ant *Atta sexdens rubropilosa* Forel.

Acid	Content [µg/gland]
(23) C_6H_5—CH_2—COOH	1—2
(24)	0.04—0.1
(25) *n*-C_7H_{15}—CHOH—CH_2—COOH	1—10
(26) *n*-C_5H_{11}—CHOH—CH_2—COOH	0.5—5.0
(27) *n*-C_3H_7—CHOH—CH_2—COOH	<0.1

Myrmicacin *(25)* is accompanied by the lower homologs *(26)* and *(27)*, which are likewise very "everyday" compounds viewed both chemically and physiologically. It only occurred to us after a comparative biochemical study of the corresponding secretions from other myrmecine species that myrmicacin

Table 3. Plant growth substances from the metathoracic glands of myrmecine ants.

Species	Myrmicacin *(25)*	Phenylacetic acid *(23)*	3-Indolylacetic acid *(24)*
Atta sexdens	+	+	+
Messor barbarus	+	+	−
Myrmica laevinodis	+	+	+
Acromyrmex subterraneus Forel	+	−	+

(25) might be an inhibitor, because the grain-gathering species *Messor barbarus*, the harvester ant, does not possess the growth regulator 3-indolylacetic acid *(24)* but does produce myrmica-

cin (Table 3). Indeed, a simple experiment showed that plum pulp can be conserved with *(25)*. Quantitative determinations of the inhibition of sporulation[*] (Table 4) also indicate that the harvester ants prevent germination of grass seeds in their granaries and the leaf-cutting ants germination of undesirable fungal spores on cultivation of their fungal gardens by means of myrmicacin. The concentration of the three carboxylic acids *(23)*, *(24)*, and *(25)* in the secretion is high enough to exert such an effect.

Table 4. Inhibition of germination [a]; compounds tested: phenylacetic acid *(23)*, 3-indolylacetic acid *(24)*, and 3-hydroxydecanoic acid (myrmicacin) *(25)*.

Spore	Conc. of inhibitor [%]	Inhibition [%] *(23)*	*(24)*	*(25)*
Botrytis cinerea	0.25	100	90	100
	0.12	100	50	100
	0,06	90	25	100
	0.03	0	0	90
Altenaria tennis	0.25	100	100	100
	0.12	100	100	100
	0.06	95	75	100
	0.03	0	0	90

[a] We are grateful to Farbwerke Hoechst AG for this test.

However, in the nest an average concentration of about 10^{-4} % is found. Ants are known to have excellent control over the conditions in their nests, and why should they not employ the same or a similar technique to lower the concentration of the constituents of their metathoracic secretion to such a level that all the carboxylic acids listed in Table 2, like true growth regulators, no longer act as inhibitors but as growth promoters? In any case, the three growth substances *(23)*, *(24)*, and *(25)* stimulate growth when present in concentrations of 10^{-4} %—as has been demonstrated by experiments with the ant fungus grown on agar[37] (cf. Table 5).

Table 5. Relative growth of the *Atta* fungus in 21 days; compounds tested: 3-indolylacetic acid *(24)*, phenylacetic acid *(23)*, and 3-hydroxydecanoic acid (myrmicacin) *(25)* [37].

	Concentration of acids in the mixtures [%]		
(24)	1.5×10^{-3}	1.5×10^{-4}	7.5×10^{-4}
(25)	1.2×10^{-3}	1.2×10^{-2}	6.0×10^{-4}
(23)	4.0×10^{-4}	3.0×10^{-4}	2.0×10^{-4}
Acids tested	Relative growth		
(24)	0	110	96
(25)	290	0	170
(23)	119	125	160
(24) + *(25)*	0	0	96
(24) + *(23)*	0	100	80
(23) + *(25)*	153	0	200
(23) + *(24)* + *(25)*	0	0	130
Control	100	100	100

We would hardly claim that the metathoracic glands of other ants also have to contain growth promoting substances; *Maschwitz*[38] has interpreted our work in that way, but concludes from the presence of a minor component, the bactericide phenylacetic acid *(23)*, which is, moreover, absent in the case of the leafcutting ant *Acromyrmex subterraneus* Forel (Table 3), that all metathoracic glands have a general bactericidal function. This generalization is not permissible, even though I would agree that every evolutionary series of defensive substances is based on substances active against the oldest enemy of all higher life forms, *i. e.* against microorganisms[1,2]. Like the long known heteroauxin *(24)*, myrmicacin *(25)* thus proved to be a plant growth regulator which should now be sought in higher or also in lower plants. However, it may be that the ants discovered myrmicacin as a growth promotor in a bygone age while it still played a role in plant metabolism, or that the fungus-growing ant is millions of years ahead of its time. While engaged in such considerations yet another thought occurred to me: might not the phenylacetic acid *(23)* be taken up by *Atta* fungus to form an antibiotic, as practiced in the case of *Penicillium* in industry. We did indeed find incorporation of ^{14}C-labeled phenylacetic acid in an antibiotic produced by the fungus[39,40], which inhibits the growth of *Staphylococcus aureus* just as well as the penicillins. It has yet to be established whether myrmicacin is also incorporated into a bactericidal and fungicidal compound.

There are probably few areas of chemical ecology where chemistry exerts such a profound influence as in the plant-fungus symbiosis just described; however, we also find another kind of co-existence in the ecology of the myrmecine ants, that of a parasite with its hosts, in which the chemistry of a Paussidae produces so much respect on the part of its host that it is allowed to feed on the most important component of the ant colony, *i. e.* on the brood. The smallest bombardier beetle that we have studied[41], *Paussus favieri*, is tolerated by the light brown ant *Pheidole pallidula* nyl. It is 4 mm long and brownish in color like its hosts. When stimulated it secretes quinones in the same way as its relatives; this can be accomplished, for example, in a glass vase and the volatile substances isolated in solution, as in our first experiments with black beetles, and concentrated by ice zone melting.

As with the Brachynidae, we again found the defensive substances *p*-benzo- und *p*-toluquinone; however, the Paussidae emit more toluquinone than benzoquinone. They accumulate the corresponding hydroquinones together with 15 % hydrogen peroxide in pygidial defensive bladders measuring only 0.3 to 0.4 mm. The myrmecophilic species *P. favieri* does not need to protect itself against external attack, that task being accomplished by the soldier caste of its hosts. Within the nest, it acquires respect by exploding quinone bombs and a certain degree of immunity lasting for a little while by virtue of the stubbornly disappearing quinone odor.

With regard to our study of the chemical ecology of insects, it is interesting that *P. favieri* is taxonomically closer to the bombardier beetles of the sub-family Brachynidae on account of its chemistry than *Arthropterus*, which *Moore* and *Wollbank* assign to the Paussidae. It remains an aim of further investigations to establish whether the Paussidae rather belong to the Brachynidae than to the Ozaenidae, or whether they even constitute a family of their own between the two. There would then be no need for the daring and improbable assumption that complicated and highly developed bombing mechanisms evolved independently in both the "Isochaeta" and the "Anisocheta" (according to *Janell*).

6. Chemical Ecology of the Araneids

We suspected a hitherto unknown antibiotic to be present in the adhesive of the mucous filaments in the webs of the

[*] We are indebted to Farbwerke Hoechst AG for this test.

garden spider (see Fig. 7), for in spite of its established protein character it resists attack by molds and bacteria for days and sometimes even for weeks even in warm and humid weather.

Fig. 7. Web of garden spider; the radial filaments are the adhesive ones.

We first found[42] the glue to be definitely acidic (pH *ca.* 4); we then noticed rhombic crystals in a droplet of glue located on a central double filament during spreading on a microscope slide. In order to analyze the spider glue we removed the surface-active glue proteins in a frothing column[43] and were then able to isolate two crystalline substances from the residue. They both displayed a paucity of IR bands typical for inorganic compounds. Accurate assignment was possible with the aid of reference spectra, according to which the first crystalline fraction is pure potassium nitrate. Its Debye-Scherrer diagram led to the same conclusion. The content of KNO_3 in the glue was determined gravimetrically as 6—8 % and that of KH_2PO_4 by colorimetry as 3 %. A third component was determined as pyrrolidone.

The trapping glue on the spiral adhesive surfaces holds the prey that has flown into the web and keeps the filaments themselves elastic. Most probably pyrrolidone, being hygroscopic, hinders drying out and KH_2PO_4 forms protons—the antibiotic sought—by dissociation, for many putrefactive bacteria avoid acidic media. However, the spiders can utilize this, the simplest of all antibiotics, to protect the protein glue against bacterial degradation only because they are able to keep the protein in solution by salting with KNO_3.

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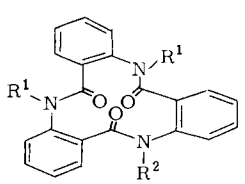
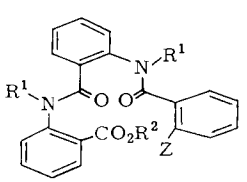
The Isolation of Conformational Diastereoisomers of *N,N',N''*-Tribenzyltrianthranilide

By *W. David Ollis, Julia Stephanidou Stephanatou, J. Fraser Stoddart*, and *Anthony G. Ferrige*[*]

Recently, we described the synthesis of *N,N',N''*-trimethyltrianthranilide *(1)*[1] and provided evidence that it crystallizes in a helical conformation, but in solution it exists in equilibrium with 5.5% of a propeller conformation[1]. We now wish to report the existence of two conformational diastereoisomers of *N,N',N''*-tribenzyltrianthranilide *(2)* as crystalline compounds.



(1), $R^1 = R^2 = CH_3$
(2), $R^1 = R^2 = CH_2C_6H_5$
(3), $R^1 = CH_2C_6H_5$; $R^2 = H$

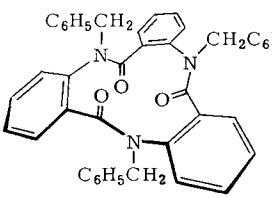


(4), $R^1 = R^2 = H$; $Z = NO_2$
(5), $R^1 = R^2 = CH_2C_6H_5$; $Z = NO_2$
(6), $R^1 = CH_2C_6H_5$; $R^2 = H$; $Z = NO_2$
(7), $R^1 = CH_2C_6H_5$; $R^2 = H$; $Z = NH_2$

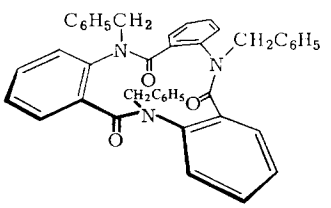
N-Benzylation ($C_6H_5CH_2Br$; NaH; THF) of *N*-[4-(2-nitrobenzoylamino)benzoyl]anthranilic acid *(4)*[2], m.p. 224°C (224°C[2]) afforded a mixture (yield >90%) of the ester *(5)* and the acid *(6)*. Reduction[3] of this mixture with $TiCl_3$ and completion of the de-esterification with LiOH yielded the *N,N'*-dibenzyl derivative *(7)* (64%, m.p. 177—179°C).

Cyclization (dicyclohexylcarbodiimide in CH_2Cl_2) of *(7)* gave *N,N'*-dibenzyltrianthranilide *(3)* (50%, m.p. 177—179°C; $\tau_{A1} = 5.00$, $\tau_{B1} = 5.54$, $J_{A1B1} = 14.7$ Hz; $\tau_{A2} = 5.17$, $\tau_{B2} = 5.33$, $J_{A2B2} = 14.8$ Hz in $CDCl_3$ for the constitutionally heterotopic benzylic-methylene protons[4, 5]). *N*-Benzylation ($C_6H_5CH_2Br$; NaH; THF) of *(3)* gave two diastereomeric products—*(2a)* and *(2b)*—with the constitution of *N,N',N''*-tribenzyltrianthranilide *(2)*. Preparative TLC on silica gel at +5°C using ethyl acetate/light petroleum (b.p. 60—80°C) (1:1) as developing solvent yielded *(2a)* (m.p. 134—144°C[6], 93% diastereomerically enriched) and *(2b)* (m.p. 260—263°C, >98% diastereomerically pure). Compound *(2a)* is the kinetically-controlled product and compound *(2b)* is the thermodynamically-preferred product.

When a ^{1}H-NMR spectrum of *(2a)* was recorded *immediately* after the crystals had dissolved in $CDCl_3$, three equal-intensity AB systems ($\tau_{A1} = 4.67$, $\tau_{B1} = 5.50$, $J_{A1B1} = 16.4$ Hz; $\tau_{A2} = 4.93$, $\tau_{B2} = 5.34$, $J_{A2B2} = 13.8$ Hz; $\tau_{A3} = 5.04$, $\tau_{B3} = 5.39$, $J_{A3B3} = 15.8$ Hz) were observed for the benzylic-methylene protons[4] of the 93% enriched diastereoisomer. In a similar experiment one AB system ($\tau_A = 3.96$, $\tau_B = 5.32$, $J_{AB} = 14.4$ Hz) was observed for the benzylic-methylene protons of *(2b)*. Diastereoisomers *(2a)* and *(2b)* interconvert slowly at room temperature in $CDCl_3$ giving eventually an equilibrium ratio [*(2a)*:*(2b)* = 41:59].



(8), Helix



(9), Propeller

The spectra of *(2a)* and *(2b)* can be rationalized in terms of two non-planar conformations, the Helix (H) *(8)* with C_1 symmetry and the Propeller (P) *(9)* with C_3 symmetry, which are formally interconverted by torsion about the Ar—N($CH_2C_6H_5$) and Ar—CO single bonds of *trans*-amide linkages. The interconversion between H and P conformations *(8)* and *(9)*, and their enantiomers (denoted as H* and P*) involves the following equilibrium: P⇌H⇌H*⇌P*.

It follows from the spectra that *(2a)* can be assigned to the Helix *(8)* with three diastereotopic benzylic-methylene groups and *(2b)* to the Propeller *(9)* with homotopic benzylic-methylene groups. The rate of diastereoisomerization of *(8)* to *(9)* was measured[7] in CD_3SOCD_3 at 63°C by monitoring the relative intensities of the benzylic-methylene proton signals in the ^{1}H-NMR spectrum as a function of time. An equilibrium constant of 0.59 and values for $\Delta G^{\ddagger}_{H\to P}$ and $\Delta G^{\ddagger}_{P\to H}$ of 24.3 and 24.8 kcal mol^{-1} were obtained for P⇌H interconversion at 63°C. The ^{1}H-NMR spectrum of the equilibrated sample of *(2)* showed temperature dependence. As the temperature is raised the signals for the Helix *(8)* decrease rapidly in relative intensity and are undetectable at 163°C. Between 163°C and 183°C the AB system for the Propeller *(9)* begins to undergo sufficient line broadening to permit line shape analysis and calculation of a value for $\Delta G^{\ddagger}_{P\rightleftharpoons P^*}$ of 26.2 kcal mol^{-1}.

The characterization of Helix *(8)* and Propeller *(9)* as crystalline diastereomeric conformational isomers is novel and represents the first example within this class of compound. It is also significant that the Helix *(8)* forms a 1:1 clathrate with ethanol[8].

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(2a). 57674-83-6: *(2b)*. 57759-54-3: *(3)*. 57674-84-7: *(4)*. 57674-85-8: *(5)*. 57674-86-9: *(6)*. 57674-87-0: *(7)*. 57674-88-1

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[5] The ^{1}H-NMR spectrum of *(3)* showed no temperature dependence below room temperature down to -100 °C, but above room temperature the two AB systems coalesced to give two singlets ($\Delta G^{\neq} = 22.6$ kcal mol^{-1} for the ring inversion process).
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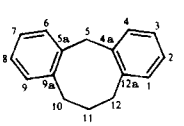
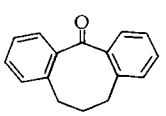
The Conformational Behavior of 5,10,11,12-Tetrahydrodibenzo[*a*,*d*]cyclooctene

By *Farouk Eltayeb Elhadi, W. David Ollis*, and *J. Fraser Stoddart*[*]

The conformational properties of 1,5-cyclooctadiene[1–4] and its derivative 5,6,11,12-tetrahydrodibenzo[*a*,*e*]cyclooctene[4–7] have been studied recently. Although the possibility of the existence of more than one conformation of 1,4-cyclooctadiene has been discussed[1] from a theoretical standpoint and the conformational behavior of some heterocyclic analogs of 5,10,11,12-tetrahydrodibenzo[*a*,*d*]cyclooctene *(1)* has been examined[8] by temperature-dependent ^{1}H-NMR spectroscopy and molecular mechanics, no experimental data are available for either of these hydrocarbons. We are now able to discuss in some detail the conformational behavior of the hydrocarbon *(1)*.



(1)



(2)

(1), m.p. 79—80 °C, was obtained by reduction ($AlCl_3$/$LiAlH_4$) of the ketone *(2)*[9], m.p. 145—148 °C (m.p. 148—149 °C[9]). At -5 °C, the ^{1}H-NMR spectrum of *(1)* in $CDCl_3$ showed an AB system ($\tau_{A1} = 5.72$, $\tau_{B1} = 6.32$, $J_{A1B1} = 12.5$ Hz) for the 5-CH_2 protons which exhibited selective broadening of the B portion of the spectrum. As the temperature was raised the unsymmetrical AB system coalesced to give a broad singlet above room temperature. Decreasing the temperature resulted in the AB system becoming well-resolved and assuming a symmetrical character. Although no signals were observed at -30 °C for a minor rapidly inverting conformation, line shape analysis with a program[8] suitable for simulating NMR line shapes of two AB systems (A1B1 and A2B2) undergoing exchange of nuclei between pairs of sites A1 and B1, A2 and B2, A1 and A2, and B1 and B2 was carried out (Table 1) successfully on selected spectra obtained between

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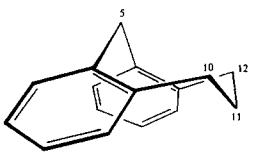
Table 1. Site exchanges, rate constants, and free-energies of activation for conformational changes in hydrocarbon *(1)* in $CDCl_3$.

Site exchanges [a]		A1→A2 B1→B2	A1⇌B1
Rel. population. $p_1 : p_2$		0.98:0.02	
k [s^{-1}]	− 5 °C	4.0	2.0
	+ 7 °C	14.0	7.0
	+19 °C	46.0	23.0
	+29 °C	102	51
	+42 °C	326	163
$\Delta G^{\neq}$ kcal/mol [b]		14.9±0.2	15.3±0.2
Process		C→TB	C⇌C*

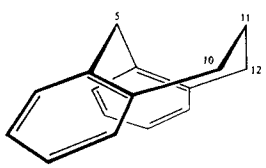
[a] The AB system A1B1 refers to the 5-CH_2 protons of the major conformation (chair, *(3)*) and A2B2 to the minor conformation (twist boat, *(5)*). At all temperatures, it was assumed that k [A2⇌B2]→∞.
[b] Average values (kcal/mol) over the temperature range −5 °C to +42 °C.

−5 °C and +42 °C assuming 2.0 % of a minor rapidly inverting conformation resonating as a singlet at $\tau_{A2B2} = 5.65$ (Table 1). Indisputable evidence for the presence of interconverting diastereomeric conformations of *(1)* in $CDCl_3$ was obtained



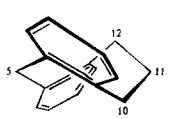
C (+−+−+−)
C* (−+−+−+)

(3)



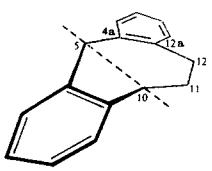
B (++−−+−)
B* (−−++−+)

(4)



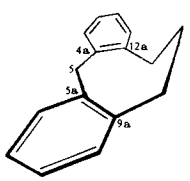
TB (+−−+−−)
TB* (−+++−+)

(5)



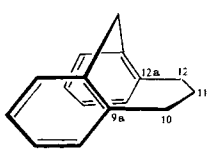
TS1A (00+−+−)
TS1A* (00−+−+)
TS1B (+−00+−)
TS1B* (−+00−+)

(6)



TS2 (−+−+00)
TS2* (+−+−00)

(7)



TS3 (+00−+−)
TS3* (−00+−+)

(8)

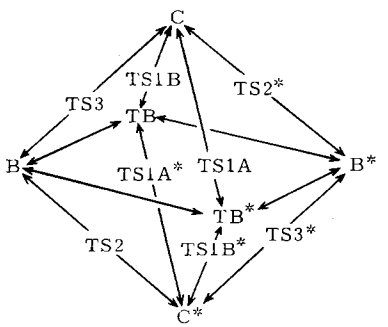


Fig. 1. Conformational changes in 5,10,11,12-tetrahydrodibenzo[*a*,*d*]cyclooctene *(1)*. The notation [7] for torsional angles refers in turn to the 12a-12, 12-11, 11-10, 10-9a, 5a-5, and 5-4a bonds.

from the temperature-dependent noise-decoupled ^{13}C-NMR spectra. The broad resonance ($\delta^{TMS}=37.6$ ppm) observed at +27 °C for C-10 and C-12 became a sharp singlet when the temperature was increased to +40 °C and also when it was decreased to −20 °C. At low temperatures no signal was observed which could be assigned to a minor conformation confirming its low population relative to that of the major conformation.

Table 2. Calculated strain energies of various conformations of the hydrocarbon *(1)*. The following energy terms have been used: E_r (bond length strain), E_θ (angle strain), E_ϕ (torsional strain), E_δ (out-of-plane strain in aromatic rings), E_{nb} (non-bonded interactional strain). Total strain energy, $E_T=E_r+E_\theta+E_\phi+E_\delta+E_{nb}$. For force constants and other empirical parameters, see Refs. [7] and [8].

Conformation	$\phi_{12,11}$ [°]	$\phi_{11,10}$ [°]	E_r	E_θ	E_ϕ	E_δ [kcal/mol]	E_{nb}	E_T
C *(3)*	− 91.8	+ 91.9	0.04	1.11	3.34	0.08	−0.57	4.00 [d]
B *(4)*	+ 75.0	− 75.0	0.15	7.80	0.83	0.08	0.44	9.30
TB *(5)*	− 58.3	− 59.6	0.08	2.75	0.54	0.39	0.25	4.01 [e]
TS1 *(6)* [a]	0.0	+ 60.8	0.36	14.99	3.03	0.06	1.13	19.57 [d]
TS2 *(7)* [b]	+108.0	−110.0	0.58	20.83	5.55	0.06	−0.08	26.94
TS3 *(8)* [c]	0.0	0.0	0.31	15.44	7.01	1.12	−0.29	23.59

[a] Defined by holding atoms 10, 11, 12, 12a, 4a, and 5, coplanar.
[b] Defined by holding atoms 12a, 4a, 5, 5a, and 9a coplanar.
[c] Defined by holding atoms 9a, 10, 11, 12, and 12a coplanar.
[d] If the difference in strain energies between the C conformation *(3)* and the TS1 conformation *(6)* is equated with $\Delta H^{\neq}$ then an approximate estimate for $\Delta G^{\neq}_{calc}$ of 15.2 kcal/mol follows from recognizing that the transition state is favored on entropy of mixing grounds by $R\ln 2$ cal K^{-1} mol^{-1} (*i.e.* there are two equivalent pathways for C→TB interconversion involving chiral transition states).
[e] The calculation on the TB conformation *(5)* allowed loss of C_2 symmetry during the energy minimization procedure. The values for $\phi_{12,11}$ and $\phi_{11,10}$ indicate that the minimum energy boat conformation corresponds to a slightly distorted TB conformation *(5)*.

Conformational analysis (Fig. 1) and strain energy calculations (Table 2) focus attention on the following conformations: (i) a rigid chair conformation [C, *(3)*, C_s symmetry], (ii) a boat conformation [B, *(4)*, C_s symmetry], (iii) a twist-boat conformation [TB, *(5)*, C_2 symmetry], and (iv) transition state conformations [TS1, *(6)*, C_1 symmetry], [TS2, *(7)*, C_s symmetry], and [TS3, *(8)*, C_s symmetry]. The calculations demonstrate that the C and TB conformations [*(3)* and *(5)*] correspond to ground state conformations and that relatively low energy transition states (B and B*) are associated with TB⇌TB* inversion while relatively high energy transition states (TS1 and TS1*) are associated with C⇌TB and C*⇌TB* interconversions necessary for C⇌C* inversion. On the basis of this analysis, the major conformation identified by NMR spectroscopy was assigned to the rigid chair conformation *(3)* and the minor conformation to the twist-boat conformation *(5)*.

The rate constants and free energies of activation for C⇌C* inversion and C→TB interconversion at various temperatures are given in Table 1. The fact that $k_{C\rightleftharpoons C^*}=0.5\,k_{C\rightarrow TB}$ is consistent with the presence of intermediate TB conformations *(5)* in the C⇌C* inversion process. The average free energy of activation ($\Delta G^{\neq}=14.9$ kcal/mol) for the C→TB interconversion is in very satisfying agreement with the calculated value (Table 2) of 15.2 kcal/mol between the C *(3)* and TS1 *(6)* conformations.

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Crystal Structure of a Platinum Complex Containing NCl_2 Ligands: $[Pt(NH_3)_3(NCl_2)_2Cl]Cl$[**]

By *Mathias Zipprich, Hans Pritzkow*, and *Jochen Jander*[*]

Reaction of $[Pt(NH_3)_5OH]Cl_3$ with chlorine leads, according to *Kukushkin*[1], to orange-red $[Pt(NH_3)_3(NCl_2)_2Cl]Cl$ *(1)*. This compound can also be obtained in a crystalline form more suitable for X-ray structure analysis by chlorinating very dilute solutions of $[Pt(NH_3)_5Cl]Cl_3$[2]. Hitherto, only the structure of a complex containing one NCl ligand was known: Cl_3VNCl[3] contains a metal-nitrogen double bond; the V—N—Cl grouping is almost linear; the N—Cl distance of 159 pm is distinctly shorter than a N—Cl single bond. We have now solved the crystal structure of *(1)* in order to determine the geometry of the NCl_2 ligand and to compare the bonding of these two groups.

The intensities of 1550 reflections (390 classified as unobserved) were measured with an automatic Weissenberg diffractometer ($Mo_{K\alpha}$, graphite monochromator, ω scan). The structure was solved by Patterson and difference Fourier syntheses and refined with anisotropic temperature factors to an R value of 0.086, weighted R value 0.061. Unit cell: space group $P2_1/c$ (C_{2h}^5): $a=1352.9(1)$, $b=1080.0(1)$, , $c=860.1(1)$ pm; $\beta=114.33(7)°$; $d_{exp}=2.77$, $d_{calc}=2.77\,g\,cm^{-3}$; $Z=4$.

The crystal structure of *(1)* is built up from $[Pt(NH_3)_3(NCl_2)_2Cl]^+$ and Cl^- ions. A cation is shown in Fig. 1. No intermolecular interactions take place between the individual ions. The platinum atom is octahedrally coordinated (bond angles 90 ± 5 and 180 ± 7°). The two NCl_2 groups are arranged *cis* to one another. The distances in the cation correspond to those in similar structures. The distances from the platinum atom to the two *trans* nitrogen atoms N3 and N4 are somewhat shorter than the distance to the nitrogen atom N5, which is arranged *trans* to one of the NCl_2 groups.

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

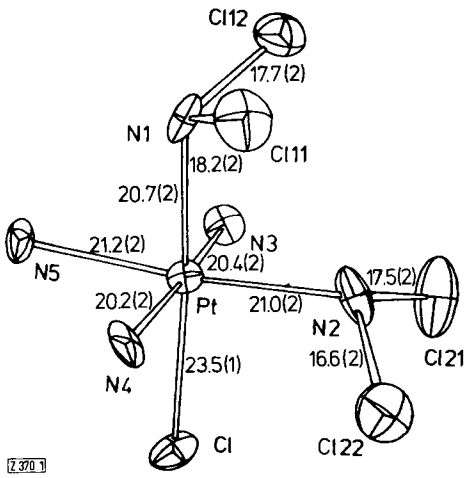

Fig. 1. Structure of the complex cation $[Pt(NH_3)_3(NCl_2)_2Cl]^+$; distances in [$10^1$ pm = 10^{-11} m].

The angles at the nitrogen atoms N1 and N2 of the two NCl_2 ligands are $108 \pm 6°$, thus indicating that the nitrogen atoms are sp^3 hybridized. The Pt—N distances to these two atoms lie in the same range as for NH_3 ligands. Hence, in contrast to the NCl group in Cl_3VNCl the NCl_2 groups here are linked to the central atom by a single bond.

The N—Cl distances scatter relatively largely (166—182 pm), but the values lie in the range which one would expect for a N—Cl single bond (NCl_3: 174 pm[4])[5].

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German version: Angew. Chem. *88*, 225 (1976)

CAS Registry number:
$[Pt(NH_3)_3(NCl_2)_2Cl]Cl$. 58408-07-4

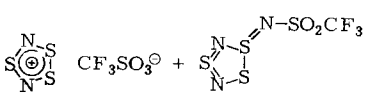
[1] *Y. N. Kukushkin*, J. Inorg. Chem. (USSR) 5, 1943 (1960).
[2] *J. Jander* and *G. Ohler*, unpublished.
[3] *J. Strähle* and *H. Bärnighausen*, Z. Anorg. Allg. Chem. *357*, 325 (1968).
[4] *H. Hartl*, *J. Schöner*, *J. Jander*, and *H. Schulz*, Z. Anorg. Allg. Chem. *413*, 61 (1975).
[5] All distances given in [pm] in the German version of this communication [Angew. Chem. *88*, 225 (1976)] should be multiplied by a factor of 10.

Synthesis of the $S_3N_2^+$ Radical Cation[**]

By *Herbert W. Roesky* and *Abbas Hamza*[*]

The metallic properties of the sulfur-nitrogen polymer $(SN)_x$ have recently attracted considerable attention[1]. Polythiazyl crystals of this kind are formed from S_2N_2, which is obtained by pyrolysis of S_4N_4; polymerization proceeds *via* a paramagnetic intermediate that has not yet been characterized. S_2N_2 is described as a highly explosive substance. By reaction of S_4N_4 with trifluoromethanesulfonic anhydride in methylene chloride we have now accomplished the first isolation of the SN radical cation as the trifluoromethanesulfonate *(1)* in an extremely facile and safe procedure[6]:

$$S_4N_4 + CF_3SO_2OSO_2CF_3 \longrightarrow$$



$CF_3SO_3^{\ominus}$ +

(1) *(2)*

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

In the reaction a small amount of $S(NSO)_2$ is also formed. The yellowish brown compound *(2)* which can be separated from the reaction mixture by sublimation or by digestion with light petroleum was found to be identical with the product of reaction between S_3N_2O and $CF_3SO_2—N=S=O$[2].

The blackish brown compound *(1)* can be purified by recrystallization from acetonitrile. Elemental analysis confirms the empirical formula. In the mass spectrum only $CF_3N_2O_3S_2$ is observed as ion of highest mass ($m/e = 241$) on fast heating because *(1)* does not volatilize without decomposition. The ESR spectrum shows the 1:2:3:2:1 quintet expected for two equivalent ^{14}N atoms ($a_N = 3.15$G, g factor 2.011)[3]. In the ^{19}F-NMR spectrum the pronounced effect of the spin density of the unpaired electron on the relaxation of the fluorine nucleus is manifested in the large half-width of the signal ($\delta_F = +76.7$ ppm, $CFCl_3$ as external standard). X-ray structure analysis of *(1)* is in progress[4].

Procedure:

Trifluoromethanesulfonic anhydride (7.6 g) is added dropwise with exclusion of moisture to a stirred suspension of S_4N_4 (5 g) in dry CH_2Cl_2. After refluxing (3 h) the solvent is removed *in vacuo*. The residue can be partly sublimed at 65 °C/0.02 torr (oil bath temperature); resublimation at 45 °C/0.02 torr affords 3.4 g of *(2)*. The nonsublimable portion is extracted with warm acetonitrile; on cooling to 0 °C lustrous blackish brown needles of *(1)* (1.8 g) precipitate[5].

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Revised: February 12, 1976 [Z 371 IE]
German version: Angew. Chem. *88*, 226 (1976)

CAS Registry numbers:
(2). 58355-86-5: S_4N_4. 28950-34-7: $CF_3SO_2OSO_2CF_3$. 358-23-6

[1] *A. G. MacDiarmid*, *C. M. Mikulski*, *P. J. Russo*, *M. S. Saran*, *A. F. Garito*, and *A. J. Heeger*, J. C. S. Chem. Comm. *1975*, 476; Chem. Eng. News *53* (21), 18 (1975).
[2] *H. W. Roesky* and *G. Holtschneider*, Chem. Ber., in press.
[3] Cf.: *S. A. Lipp*, *J. J. Chang*, and *W. L. Jolly*, Inorg. Chem. *9*, 1970 (1970); *R. Appel*, *M. Montenarh*, and *I. Ruppert*, Chem. Ber. *108*, 582 (1975). – We are indebted to Prof. *H. Bock* and Dipl.-Chem. *G. Brähler*, Universität Frankfurt for performing the measurements.
[4] Prof. *B. Krebs*, Universität Bielefeld.
[5] It is difficult to obtained the crystals completely free from acetonitrile. After recrystallization *(1)* has the composition $CF_3N_2O_3S_4 \cdot \frac{1}{2}CH_3CN$. The molecular formula originally given [Nachr. Chem. Tech. *24*, 25 (1976)], $CF_3N_2O_3S_3$ corresponds to a degradation.
[6] *Note added in proof* (February 20, 1976): The $S_3N_2^+$ ion has been prepared independently by *R. J. Gillespie*, *P. R. Ireland*, and *J. E. Vekres*, Can. J. Chem. *53*, 3147 (1975).

Cyclobutadiene—A Square Singlet Molecule?[1][**]

By *Günther Maier*, *Hans-Georg Hartan*, and *Tugmac Sayrac*[*]

The matrix isolation technique, first successfully employed in the study of alkyl-substituted cyclobutadienes[2], also permits isolation and spectroscopic investigation of the unsubstituted parent compound *(2)* in monomeric form. Starting from the Corey lactone *(3)*, *Krantz*[3] and *Chapman*[4] were

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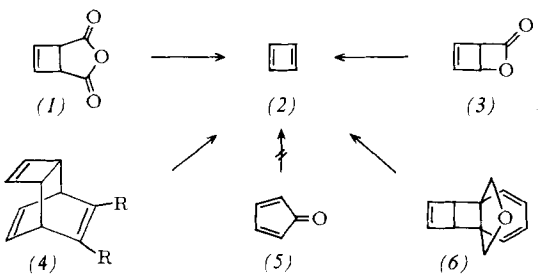
able to generate *(2)* in an argon matrix at 8K and to record its IR spectrum. *Masamune*[5] photolyzed the ether *(6)* and we[6] photocleaved the anhydride *(1)* in organic glasses at 77 K and also deduced the formation of monomeric cyclobutadiene.



(1) *(2)* *(3)* *(4)* *(5)* *(6)*

(4a), R = H *(4c)*, R = $COOCH_3$

(4b), R-R = -CH=CH-CH=CH- *(4d)*, R-R = -CO-O-CO-

The number of observed IR bands [square geometry (D_{4h}) allows four IR-active vibrations, and a rectangular geometry (D_{2h}) seven] requires that *(2)* has a square structure. However, most theoretical calculations predict that square cyclobutadiene should have a triplet ground state and that the energy content should increase in the order RS (rectangular singlet), ST (square triplet), SS (square singlet). On the other hand, the chemistry of *(2)* suggests a singlet molecule. On the basis of MINDO/3 calculations, *Dewar*[7] has proposed the following solution of this dilemma: Photocleavage of *(3)* should afford *(2)* in an excited triplet state which, owing to a barrier of 3.5 kcal/mol to the transition of ST to RS cyclobutadiene, is expected to be stable under matrix conditions.

In the present communication we shall demonstrate that the interpretation of the IR spectra of *(2)*[3,4] requires modification and that the tendency of cyclobutadiene to form complexes must also be considered in any discussion of its properties.

Irradiation of the anhydride *(1)* in an argon matrix at 7 K with a low pressure mercury lamp leads essentially to the same IR spectrum[3,4] as is observed on photofragmentation of *(3)*. There is, however, one striking difference: the band at 1240 cm^{-1} is now split into a doublet (1237, 1241 cm^{-1}) (Table 1).

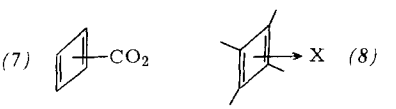
This finding is in itself rather odd, because more bands appear than would be permissible for a single D_{4h} species. The results of photofragmentation of compounds of type *(4)* give even more reason for scepticism.

Table 1. Comparison of the IR spectra [cm^{-1}] obtained on irradiation of the cyclobutadiene precursors *(1)*, *(3)*, and *(6)*. On cleavage of *(3)* the bands of CO_2 also appear (2340, 660 cm^{-1}) and in the case of *(1)* those of CO_2 and CO (2138 cm^{-1}).

(1)	*(3)*		*(6)*	calc. (D_{4h})
	[3]	[4]		
—	—	3040	—	3000 (E_u)
1241 + 1237	1238	1240	1240	1236 (E_u) [3b]
653	653	650	—	661 (E_u)
573	573	570	570	576 (A_{2u})

While the hydrocarbons *(4a)* and *(4b)* are photostable, the ester *(4c)* and the anhydride *(4d)* undergo cleavage on irradiation (argon, 7 K, 254 nm). The presence of only small amounts of cyclobutadiene can be deduced from the IR spectra (1240, 570 cm^{-1}). Nevertheless, it can be clearly seen that a "cyclobutadiene band" at 653 cm^{-1} is absent. The same peculiarity is also evident in the IR spectrum recorded on analogous photocleavage of the ether *(6)*[8] (Table 1). Only two intense absorptions are again observed at 570 and 1240 cm^{-1} which must be due to cyclobutadiene because they disappear in favor of the bands due to the *syn* dimer of *(2)* on thawing to 32 K. No band appears at 653 cm^{-1}.

How can these results be rationalized? We believe that photochemical cleavage of *(3)* affords neither free SS nor ST cyclobutadiene in the inert gas matrix but instead a species of type *(7)* associated with CO_2.



(7) *(8)*

The band at 653 cm^{-1} is not assignable to cyclobutadiene but to CO_2 functioning as a ligand whose deformation vibration splits into a doublet (660, 653 cm^{-1}) on destroying the degeneracy as a result of complex formation[9,10]. Confirmatory evidence comes from the observation that these two bands on complete photochemical secondary cleavage into two acetylene molecules do not disappear because a corresponding associate exists between acetylene and CO_2. Interestingly, the association has a fairly pronounced effect in the CO_2 ligand but is hardly noticeable in the substrate molecule cyclobutadiene.

In analogy to the preparation of "free" tetramethylcyclobutadiene from the tetramethyl derivative of *(6)*[11] formation of nonassociated cyclobutadiene would appear most likely on cycloreversion of the ether *(6)*. It may be deduced from the result of that cleavage that free cyclobutadiene *(2)* only gives two bands that are intense enough to be observed in the IR spectrum. In accord with calculations[3b], these can be assigned to the ring- and out-of-plane C—H deformation vibrations of a cyclobutadiene molecule having D_{4h} symmetry. In other words: the number of observed IR absorptions cannot

1240 cm^{-1} (E_u) 570 cm^{-1} (A_{2u})

serve for assignment to a square geometry. The only valid argument in favor of a square geometry is that the band at 1238 cm^{-1} must be split on deformation[3b]. The double band observed on irradiation of the anhydride *(1)* (1241, 1237 cm^{-1}) probably has a different origin. The difference of 4 cm^{-1} is too small. The splitting is presumably explained by the presence of two kinds of cyclobutadiene: cyclobutadiene associated with CO_2 together with free or CO-complexed cyclobutadiene. In order to examine the second possibility we have—in analogy to the preparation of tri-*tert*-butylcyclobutadiene[12]—generated cyclopentadienone *(5)* in an argon matrix[13] and attempted to cleave this product to *(2)* and CO. Under these conditions, however, cyclopentadienone is photostable.

The tendency of *(2)* to undergo association has its parallels in the excellent donor properties of tetramethylcyclobutadiene[11] [formation of charge-transfer complexes of type *(8)*] and in the strongly basic or nucleophilic behavior of tri-*tert*-butylcyclobutadiene[14]. The unsubstituted parent compound thus fits well into the pattern of the known properties of alkyl-substituted cyclobutadienes. All presently known properties of *(2)* are in accord with a recently published theoretical treatment by *Borden*[15] which states that cyclobutadiene, contrary to all previous predictions[2,7,16], can have a singlet

ground state even in a square or at least *effectively* square geometry.

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German version: Angew. Chem. 88, 252 (1976)

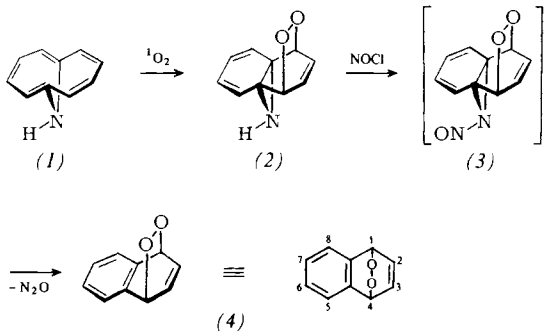
CAS Registry numbers:
(1). 10374-07-9: *(2)*. 1120-53-2: *(3)*. 22980-23-0: *(6)*. 58343-27-4

[1] Small Rings, Part 18.—Part 17: ref. [14].
[2] Survey: *G. Maier*, Angew. Chem. *86*, 491 (1974); Angew. Chem. Int. Ed. Engl. *13*, 425 (1974).
[3] a) *C. Y. Lin* and *A. Krantz*, J. Chem. Soc. Chem. Commun. *1972*, 1111; b) *A. Krantz, C. Y. Lin*, and *M. D. Newton*, J. Am. Chem. Soc. *95*, 2744 (1973).
[4] a) *O. L. Chapman, C. L. McIntosh*, and *J. Pacansky*, J. Am. Chem. Soc. *95*, 614 (1973); b) *O. L. Chapman, D. De La Cruz, R. Roth*, and *J. Pacansky, ibid. 95*, 1337 (1973).
[5] *S. Masamune, M. Suda, H. Ona*, and *L. M. Leichter*, J. Chem. Soc. Chem. Commun. *1972*, 1268.
[6] *G. Maier* and *B. Hoppe*, Tetrahedron Lett. *1973*, 861.
[7] *M. J. S. Dewar* and *H. W. Kollmar*, J. Am. Chem. Soc. *97*, 2933 (1975).
[8] Prepared according to *H.-D. Martin* and *M. Hekman*, Synthesis *1973*, 667.
[9] The reports on partially deuterated cyclobutadienes [3b, 4b] and in particular the interpretation of the IR spectrum of monodeuterated *(2)* [3b] also have to be revised. If it is correct that a band appears at 655 cm^{-1} due to *(2)* on irradiation of pyridine in an argon matrix [4a] then this band cannot arise from CO_2 but must have its origin in the ability of simultaneously formed hydrogen cyanide to undergo complex formation. The additional absorption observed in the photocleavage of pyridine as well as of *(1)* or *(3)* should be assigned to a deformation vibration that becomes IR active on transition ($E_g \rightarrow E$) from *(2)* (D_{4h}) to a complex of type *(7)* (C_{4v}). We have attempted to repeat (Ar; 7 K; 254 or > 300 nm) the preparation of cyclobutadiene from pyridine (experiments by *U. Schäfer*) and found two bands of very low intensity at 570 and 1240 cm^{-1}, but none at 655 cm^{-1}.
The UV spectroscopic findings are not very informative: photocleavage (Ar, 7 K, 254 nm) of *(1)* and *(3)* gives no pronounced maxima (only end absorption, beginning at about 290 nm). On irradiation of *(6)* only the UV bands of phthalan (265, 272 nm) can be observed. UV-absorptions formerly (Refs. [2], [3a], [5], [6]) assigned to *(2)* therefore must arise from other species.
[10] We are indebted to Prof. *K. Dehnicke* for his help in the interpretation of the IR spectra.
[11] *G. Maier, W. Mayer, C. Haacke*, and *R. Askani*, Angew. Chem. *85*, 1057 (1973); Angew. Chem. Int. Ed. Engl. *12*, 1061 (1973).
[12] *G. Maier* and *A. Alzérreca*, Angew. Chem. *85*, 1056 (1973); Angew. Chem. Int. Ed. Engl. *12*, 1051 (1973).
[13] The existence of *(5)* has been established by rapid pyrolysis of suitable precursors and trapping of the pyrolysis products in an IR cell cooled to 77 K: *O. L. Chapman* and *C. L. McIntosh*, J. Chem. Soc. Chem. Commun. *1971*, 770. Pure cyclopentadienone is obtainable in the following way: *o*-benzoquinone is irradiated in an argon matrix at 7 K with light > 300 nm. Cleavage of the bond between the two carbonyl groups quantitatively affords the corresponding bisketene. Secondary irradiation with 254-nm light then yields CO and cyclopentadienone (IR: 1725, 1721, 1328, 1130, 970, 920, 815 cm^{-1}).
[14] *G. Maier* and *W. Sauer*, Angew. Chem. *87*, 675 (1975); Angew. Chem. Int. Ed. Engl. *14*, 648 (1975).
[15] *W. T. Borden*, J. Am. Chem. Soc. *97*, 5968 (1975).
[16] *W. J. Hehre* and *J. A. Pople*, J. Am. Chem. Soc. *97*, 6941 (1975).

Naphthalene 1,4-Endoperoxide

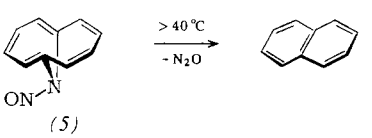
By *Maria Schäfer-Ridder, Ulrich Brocker*, and *Emanuel Vogel*[*]

In contrast to anthracene and higher members of the acene series[1], naphthalene shows hardly any tendency to react with singlet oxygen ($^1O_2$) to form a 1,4-endoperoxide[2]; it was estimated from kinetic data that naphthalene has a reactivity index for addition of $^1O_2$ which is several degrees of magnitude lower than that of the acenes[3]. In fact, the synthesis of the endoperoxide *(4)* from naphthalene and $^1O_2$ appears to be obstructed primarily by the high activation energy of the addition, and not at all by any great tendency of *(4)* to decompose, for we have now found an alternative entry to this compound.



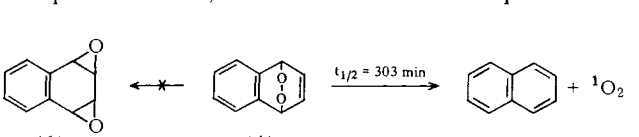
The *N*-nitrosoaziridine *(3)* of the 1,4-endoperoxide *(2)*[4] obtainable from 1,6-imino[10]annulene *(1)*[5] already eliminates N_2O at very low temperature[6]. Treatment of *(2)* dissolved in methylene chloride in the presence of triethylamine at −78 °C with an excess of liquid nitrosyl chloride (duration of reaction 1 h) affords *(4)*, which is isolated, after conventional workup with cooling (0–5 °C) and recrystallization from acetone (−20 °C), as colorless needles (rapid decomposition above room temperature); 50 % yield.

Attempts to prepare *(4)* by way of *N*-nitroso-1,6-imino[10]annulene *(5)* [pale yellow needles (from CH_2Cl_2/hexane), m.p. ≈70 °C (dec.); ^{1}H-NMR (CD_2Cl_2): multiplet at $\tau = 1.9$—2.9; UV (methanol): $\lambda_{max} = 250$ ($\varepsilon = 49000$), 295 (6350), 376 (240), 388 (380), 398 (630), 409 nm (720)], smoothly formed on reaction of *(1)* with nitrosyl tetrafluoroborate in acetonitrile, did not lead to the desired goal because *(5)* failed to react with $^1O_2$. In solution, *(5)* decomposes only above 40 °C to naphthalene and N_2O.



Structural proof for naphthalene 1,4-endoperoxide (1,4-epidioxy-1,4-dihydronaphthalene) *(4)* is provided mainly by the ^{1}H-NMR spectrum [(in $CDCl_3$, TMS as internal standard): AA'BB' system with $\tau = 2.70$ (H^5, H^8) and 2.76 (H^6, H^7) ($J_{5,6} = 7.34$, $J_{5,7} = 1.17$, $J_{5,8} = 0.52$, $J_{6,7} = 7.68$ Hz) and AA'XX' system at $\tau = 3.02$ (H^2, H^3) and 4.36 (H^1, H^4) ($J_{1,2} = 5.89$, $J_{1,3} = 1.66$, $J_{1,4} = 0.99$, $J_{2,3} = 8.08$ Hz)]. The UV spectrum [(cyclohexane): $\lambda_{max} = 205$ nm ($\varepsilon = 26100$)] of the 1,4-dihydronaphthalene type and the IR spectrum [(KBr): 1655 cm^{-1} (C=C)] are in accord with structure *(4)*.

Compound *(4)*, which can be handled without difficulty, undergoes thermal cleavage to naphthalene and oxygen with comparative ease[7]; in solution the reaction is quantitative.



On insertion into the Arrhenius equation, the rate constants determined by NMR spectroscopy between 18 and 26 °C afford the activation parameters $E_A = 23.7 \pm 0.7$ kcal mol^{-1} and $\log A = 13.26 \pm 0.5$ ($\Delta H^{\neq} = 23.2 \pm 0.9$ kcal mol^{-1}, $\Delta S^{\neq} = 0.2 \pm 1.1$ cal deg^{-1} mol^{-1}) for fragmentation of *(4)*. The

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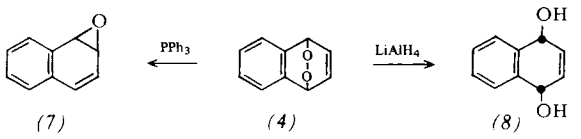
half-life of *(4)* at 20°C is 303 min. That the oxygen released by *(4)* is $^1O_2$ follows from the reaction of *(4)* with $^1O_2$ acceptors such as diphenylisobenzofuran or tetramethylethylene[8], which yields the products expected for $^1O_2$: for instance, 1 mmol of *(4)* and 0.5 mmol of 1,3-diphenylisobenzofuran in 10 ml of benzene at 20°C (24 h in the dark) furnish only *o*-dibenzoylbenzene and naphthalene in almost quantitative yield.

The temperature range in which the 1,4-endoperoxide *(4)* permits $^1O_2$ oxygenations (preferably 15—25°C) suggests a useful supplementary role alongside the known singlet oxygen sources of ozonide[9] and 1,4-endoperoxide type[1,2].



(7) *(4)* *(8)*

Reaction of *(4)* with triphenylphosphane (−78°C) leads to partial deoxygenation, the major product being *(7)*[10] (no indication was found for formation of the isomeric 1,4-epoxy-1,4-dihydronaphthalene). Reduction of *(4)* with $LiAlH_4$ in ether (0°C) gives *cis*-1,4-dihydroxy-1,4-dihydronaphthalene *(8)* [m.p. 106—107°C; NMR ($CDCl_3$): doublets at $\tau = 5.0$ (H^1, H^4) and 3.88 (H^2, H^3) and multiplet at $\tau = 2.2$—2.8 (H^5—H^8)], which has also been prepared in another way by *Jerina et al.*[11].

Compound *(8)* is a potential isolable secondary product of a biological oxidation of naphthalene to *(4)*, for which no firm evidence has yet become available. In view of the natural occurrence of 1,4-endoperoxides[12] it would hardly be surprising to find that living organisms can oxidize naphthalene not only to *(7)* but also to *(4)*. Our knowledge of the properties of *(4)* and *(8)* should facilitate solution of this problem.

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German version: Angew. Chem. *88*, 262 (1976)

CAS Registry numbers:
(1). 4753-55-3: *(2)*. 58692-15-2: *(3)*. 58692-23-2: *(4)*. 58692-24-3: *(5)*. 58692-25-4: *(7)*. 17180-88-0: *(8)*. 51096-10-7: nitrosyl chloride. 2696-92-6: nitrosyl tetrafluoroborate. 14635-75-7: triphenylphosphane. 603-35-0: lithium tetrahydridoaluminate. 16853-85-3

[1] *J. Rigaudy*, Pure Appl. Chem. *16*, 169 (1968).
[2] Experience gained so far indicates that formation of 1,4-endoperoxides on dye-sensitized photooxygenation of the naphthalene system requires the presence of electron-donating substituents such as methoxy [1] or alkyl groups (preferably in 1,4 position): *H. H. Wasserman* and *D. L. Larsen*, J. Chem. Soc. Chem. Commun. *1972*, 253; *H. Hart* and *A. Oku*, *ibid.* *1972*, 254.
[3] *B. Stevens*, *S. R. Perez*, and *J. A. Ors*, J. Am. Chem. Soc. *96*, 6846 (1974).
[4] *E. Vogel*, *A. Alscher*, and *K. Wilms*, Angew. Chem. *86*, 407 (1974); Angew. Chem. Int. Ed. Engl. *13*, 398 (1974).—Final proof for the *anti* arrangement of the NH and O—O groups of *(2)* has yet to be obtained.
[5] *E. Vogel*, *M. Biskup*, *W. Pretzer*, and *W. A. Böll*, Angew. Chem. *76*, 785 (1964); Angew. Chem. Int. Ed. Engl. *3*, 642 (1964); *E. Vogel*, *W. Pretzer*, and *W. A. Böll*, Tetrahedron Lett. *1965*, 3613.
[6] Concerning the fragmentation of *N*-nitrosoaziridines, cf. *H. Prinzbach*, *M. Breuninger*, *B. Gallenkamp*, *R. Schwesinger*, and *D. Hunkler*, Angew. Chem. *87*, 350 (1975); Angew. Chem. Int. Ed. Engl. *14*, 348 (1975); and references cited therein.
[7] No indication of the formation of the isomeric *syn*-naphthalene 1,2;3,4-dioxide *(6)* [see *E. Vogel*, *H.-H. Klug*, and *M. Schäfer-Ridder*, Angew. Chem. *88*, 268 (1976); Angew. Chem. Int. Ed. Engl. *15*, 229 (1976)] was obtained.—In contrast to *(4)*, anthracene 9,10-endoperoxide on heating does not release the O—O bridge as $^1O_2$ but instead undergoes homolysis of the O—O bond which initially gives the *syn*-1,2:3,4-diepoxide: *J. Rigaudy*, *J. Baranne-Lafont*, *A. Defoin*, and *N. Kim Cuong*, C. R. Acad. Sci. Ser. C *280*, 527 (1975).
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[10] *E. Vogel* and *F.-G. Klärner*, Angew. Chem. *80*, 402 (1968); Angew. Chem. Int. Ed. Engl. *7*, 376 (1968); *D. R. Boyd*, *D. M. Jerina*, and *J. W. Daly*, J. Org. Chem. *35*, 3170 (1970).
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[12] *K. Gollnick* and *G. O. Schenck* in *J. Hamer*: 1,4-Cycloaddition Reactions. Academic Press, New York 1967, p. 255.

syn- and *anti*-Naphthalene 1,2;3,4-Dioxide

By *Emanuel Vogel*, *Hans-Helmut Klug*, and *Maria Schäfer-Ridder*[*]

Some time ago we reported the synthesis of *syn*-benzene dioxide[1] and proved that this arene oxide is in mobile equilibrium with its eight-membered ring valence tautomer 1,4-dioxocin above 50°C. Almost simultaneously, *Borders et al.*[2] described the isolation of an antibiotic having a benzene dioxide partial structure whose stereochemistry could only be elucidated by comparison with the stereoisomeric benzene dioxides[3] as involving a *syn* arrangement of the epoxide rings. The appearance of a benzene dioxide derivative as a metabolite of microorganisms suggests that nature may also produce naphthalene oxides, especially since naphthalene monoxide has already been detected as a product of enzymatic naphthalene degradation[4]. The search for such metabolites would doubtless be facilitated by a knowledge of the parent compounds, above all *syn*- and *anti*-naphthalene 1,2;3,4-dioxide [*(1)* and *(2)*]. We have now found methods of synthesizing these two arene oxides.

(1) *(2)*

The synthesis of *(1)* exploits the photooxidation of 1,6-imino[10]annulene *(3)*. Irradiation of *(3)* with a sodium vapor lamp in the presence of methylene blue and oxygen [methylene chloride/methanol (100:1); 10—15°C; 36 h] yields the 1,4-endoperoxide *(4)*[5], which does not have to be isolated but, after removal of solvent, can be thermolyzed in boiling ethyl acetate (10 h). As may be predicted from the thermal behavior of 1,6-methano[10]annulene endoperoxide[6], *(4)* undergoes complete isomerization to the iminodioxatrishomobenzene derivative *(5)*[7] [m.p. 175—176°C (dec.); NMR ($CDCl_3$): AA'BB' systems, centered at $\tau = 3.58$ (olefin protons) and 6.53 (epoxide protons), singlet at $\tau = 10.7$ (NH proton); UV (CH_3CN): $\lambda_{max} = 255$ nm ($\varepsilon = 4650$); yield 25 % (36 % based on reacted *(3)*)]. To our knowledge, *(4)* and *(5)* are the first derivatives of the hitherto hypothetical benzene imine[8] which are unsubstituted at the aziridine nitrogen. Reaction of *(5)* with an excess of nitrosyl chloride in the presence of an equivalent amount of triethylamine in methylene chloride at −78°C leads to the unstable *N*-nitrosoaziridine *(6)* which transforms at very low temperature with elimination of N_2O into the desired *syn*-naphthalene 1,2;3,4-dioxide *(1)*. Recrystallization from ethyl acetate furnishes *(1)* as a remarkably stable colorless compound[9] (rhomboids) having m.p. 178—180°C (dec.); yield 50 %.

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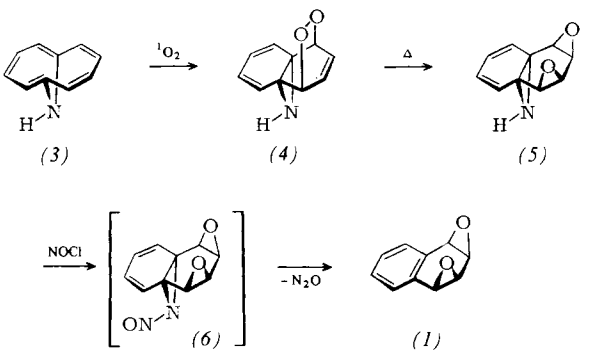
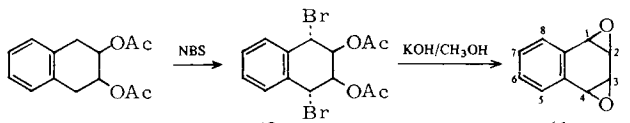
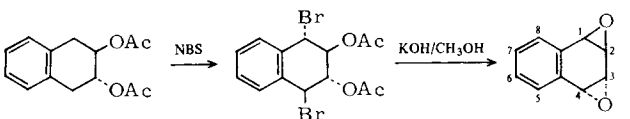


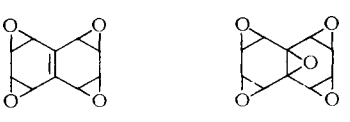
Apart from this route, *(1)* is also accessible conventionally from *(7)* *via* the naphthalene bisbromoacetate *(8)*. Compound *(8)* is a component of the complex bromination mixture arising in the reaction of *(7)* with *N*-bromosuccinimide (NBS) in boiling carbon tetrachloride. Treatment of an ethereal solution of the mixture, which was not resolved, at room temperature with 5% methanolic potassium hydroxide gives a low yield of *(1)* (5—8%).





anti-Naphthalene 1,2;3,4-dioxide *(2)* is obtained in analogous manner from *(9)* *via* the naphthalene bisbromoacetate *(10)*. After isolation by chromatography over silica gel [ether/hexane (1:1)], *(2)* crystallized as colorless needles, m.p. 99—100°C, from ether/pentane (9:1); yield 1—2%.

The NMR spectra of the naphthalene dioxides *(1)* [AA'BB' system at $\tau = 6.04$ (H^1, H^4) and 6.11 (H^2, H^3) ($J_{1,2} = 3.63$, $J_{1,3} = 0.30$, $J_{1,4} = 0.01$, $J_{2,3} = 2.97$ Hz) and AA'BB' system, centered at $\tau = 2.5$ (H^5—H^8); in [D_6]acetone] and *(2)* [AA'BB' system at $\tau = 6.06$ (H^2, H^3) and 6.34 (H^1, H^4) ($J_{1,2} = 4.22$, $J_{1,3} = 0.75$, $J_{1,4} = 0.10$, $J_{2,3} = 1.75$ Hz) and AA'BB' system, centered at $\tau = 2.6$ (H^5—H^8); in $CDCl_3$] are in full accord with those of *syn*- and *anti*-benzene dioxide, regarding the signal pattern and the coupling constants of the epoxide protons. Once more, only the vicinal coupling constant $J_{2,3}$ provides a reliable tool for distinguishing between the two stereoisomers by NMR spectroscopy. The $J_{2,3}$ coupling constants of 2.97 and 1.75 Hz, respectively, determined by analysis of the AA'BB' system of the epoxide protons, which are lower than suggested by the Karplus equation owing to the influence of the electronegative oxygen atoms[10], are almost identical with those of the corresponding benzene dioxides (2.83 and 1.75 Hz).



The photooxidation of *(3)* also proved to be a key reaction for the synthesis of a naphthalene 1,2;3,4;5,6;7,8-tetroxide *(11)* [m.p. 186°C (dec.)] whose configuration is not yet known with certainty. Starting from the intermediate *(5)* the reaction sequence of $^1O_2$ addition, thermolysis, and nitrosation leads to *(11)*. A naphthalene pentoxide *(12)* [m.p. 280°C (dec.)][11], probably *syn,syn,syn,syn*-1,2;3,4;5,6;7,8-*anti*-9,10-naphthalene pentoxide, was finally isolated as the product of "exhaustive photooxidation" of 1,6-oxido[10]annulene. The stereochemistry of *(11)* and *(12)* is currently being studied by X-ray structure analysis[12].

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German version: Angew. Chem. *88*, 268 (1976)

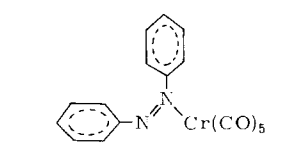
CAS Registry numbers:
(1), 58692-14-1; *(2)*, 58717-74-1; *(3)*, 4753-55-3; *(4)*, 58692-15-2; *(5)*, 58717-75-2; *(6)*, 58692-16-3; *(7)*, 58692-17-4; *(8)*, 58692-18-5; *(9)*, 58692-19-6; *(10)*, 58692-20-9; *(11)*, 58692-21-0; *(12)*, 58692-22-1; NBS, 128-08-5; nitrosyl chloride, 2696-92-6

[1] *H.-J. Altenbach* and *E. Vogel*, Angew. Chem. *84*, 985 (1972); Angew. Chem. Int. Ed. Engl. *11*, 937 (1972).
[2] *D. B. Borders*, *P. Shu*, and *J. E. Lancaster*, J. Am. Chem. Soc. *94*, 2540 (1972); *D. B. Borders* and *J. E. Lancaster*, J. Org. Chem. *39*, 435 (1974); US-Pat. 3770773 (1973).
[3] For the synthesis of *anti*-benzene dioxide see: *E. Vogel*, *H.-J. Altenbach*, and *E. Schmidbauer*. Angew. Chem. *85*, 862 (1973): Angew. Chem. Int. Ed. Engl. *12*, 838 (1973); *C. H. Foster* and *G. A. Berchtold*, J. Org. Chem. *40*, 3743 (1975).
[4] *D. M. Jerina*, *J. W. Daly*, *B. Witkop*, *P. Zaltzman-Nirenberg*, and *S. Udenfriend*, J. Am. Chem. Soc. *90*, 6525 (1968).
[5] *M. Schäfer-Ridder*, *U. Brocker*, and *E. Vogel*, Angew. Chem. *88*, 262 (1976); Angew. Chem. Int. Ed. Engl. *15*, 228 (1976).
[6] *E. Vogel*, *A. Alscher*, and *K. Wilms*, Angew. Chem. *86*, 407 (1974); Angew. Chem. Int. Ed. Engl. *13*, 398 (1974).
[7] The *anti* configuration of *(5)* assumed here still requires final proof.
[8] *syn*-Benzene triimine was described by *R. Schwesinger* and *H. Prinzbach*, Angew. Chem. *85*, 1107 (1973); Angew. Chem. Int. Ed. Engl. *12*, 989 (1973).
[9] The existence of a thermal equilibrium between *(1)* and its 1,4-dioxocin valence tautomer having *o*-quinodimethane structure could not be established, either by spectroscopy or by trapping reactions with dienophiles.
[10] *K. Tori*, *T. Komeno*, and *T. Nakagawa*, J. Org. Chem. *29*, 1136 (1964).
[11] *A. Breuer* and *E. Vogel*, unpublished experiments.
[12] Prof. *R. E. Davis*, University of Austin, Texas, is engaged in X-ray structure analyses of naphthalene polyoxides.

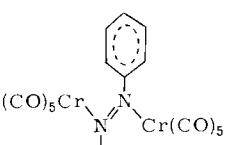
Carbonylchromium Complexes of Azobenzene[1]

By *Max Herberhold* and *Konrad Leonhard*[*]

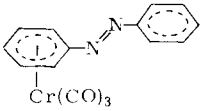
During investigations of the photo-induced and thermal reaction of azobenzene (azb) with hexacarbonylchromium we



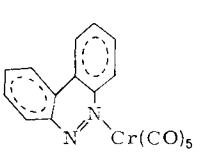
(1) (deep red)
ν(C≡O) 2063, 1984, 1941 and 1910 cm^{-1} (in THF)



(2) (blue-violet)



(3) (deep red)
ν(C≡O) 1972 and 1897 cm^{-1} (in THF)



(4) (red-brown)
ν(C≡O) 2065, 1983, 1927 and 1890 cm^{-1} (in THF)

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have been able to isolate—depending upon the reaction conditions—the three novel complexes *(1)*—*(3)*, and for the first time have observed a difference in behavior of *cis*- and *trans*-azobenzene in complex formation.

When *cis*-azobenzene is added to a photolyzed solution of $Cr(CO)_6$ in tetrahydrofuran (THF) the mononuclear complex *(1)* is formed:

$$Cr(CO)_6 \xrightarrow[-CO]{THF;\ h\nu} [Cr(CO)_5(THF)] \xrightarrow[-THF]{+\ cis\text{-azb};\ 25\,^\circ C} Cr(CO)_5(cis\text{-azb})$$
(1)

Benzo[*c*]cinnoline, which can be regarded as a rigidly fixed form of *cis*-azobenzene, reacts in an analogous way to give *(4)*[2]. *trans*-Azobenzene does not react under these conditions.

Compound *(1)* is stable in air, but sensitive to light. The mass spectrum shows the molecular ion $Cr(CO)_5(azb)^+$ ($m/e = 374$) and all the fragment ions $Cr(CO)_n(azb)^+$ ($n = 4$—0). In the electronic spectrum of *(1)* the characteristic $n \rightarrow \pi^*$ transition of *cis*-azobenzene (440 nm) is shifted to 505 nm; a new absorption appears at 390 nm.

Compound *(1)* is the first mononuclear azobenzene complex in which the azb ligand is present in the *cis* configuration[3a]. All azobenzene complexes studied so far by X-ray methods[3] always contain *trans*-azobenzene. In some cases catalyzed isomerization of *cis*- to *trans*-azobenzene was observed in the presence of metal complexes[3b].

Although *trans*-azobenzene—like *trans*-azocyclohexane[4]—does not react with a solution of $[Cr(CO)_5(THF)]$ in THF, subsequent removal of solvent and drying of the residue under high vacuum leads to formation of a dinuclear complex *(2)*, which is stable in the solid state up to *ca.* 65 °C. In the presence of solvents, *(2)* already decomposes at −40 °C with liberation of pure *trans*-azobenzene (λ_{max} 449 and 316 nm in *n*-hexane). At −20 °C a deep-red intermediate [presumably $Cr(CO)_5$(*trans*-azb)] can be observed. Decomposition of *(2)* in benzene affords solvent-stabilized $[Cr(CO)_5]$-fragments which are stable for a short period of time and can be used for the synthesis of pentacarbonylchromium complexes. The IR spectrum of *(2)* ($\nu(C\equiv O)$ 2053, 1963, 1924, and 1894 cm^{-1} in KBr) is almost identical to that of the (much more stable) tungsten complex (*trans*-azb)$[W(CO)_5]_2$ which precipitates on irradiation of a hexane solution of $W(CO)_6$ in the presence of *trans*-azobenzene.

Thermal reaction of azobenzene with $Cr(CO)_6$ in boiling diglyme at 160—170 °C leads with strong decomposition to the π-arene complex *(3)* (m.p. 121 °C) in *ca.* 1 % yield; anilinetricarbonylchromium[5] (6 %) is also formed. *(3)* is sublimable in a high vacuum above 90 °C. In the mass spectrum the molecular ion $Cr(CO)_3(azb)^+$ ($m/e = 318$) and successive loss of the three CO ligands followed by the fragmentation of the π-bonded azobenzene can be observed. The $\nu(C\equiv O)$ frequencies in the IR spectrum of *(3)* (1972 and 1897 cm^{-1} in THF) are surprisingly similar to those of benzenetricarbonylchromium (1972 and 1890 cm^{-1}); obviously the phenylazo substituent does not exert any considerable influence on the charge density in the π-bonded benzene ring. In the ^{1}H-NMR spectrum of *(3)* only the proton signals of the coordinated ring are shifted upfield (multiplets at $\tau = 3.55$ and 4.12 in $[D_6]$-acetone), while the signals of the free phenyl group occur, as in *trans*-azobenzene itself, at $\tau = 2.1$ and 2.4. *trans*-Azobenzene is liberated in the decomposition of *(3)* with bromine water.

Experimental[6]:

cis-Azobenzene-pentacarbonylchromium (1)

A solution of $Cr(CO)_6$ (0.22 g, 1 mmol) in THF (100 ml) is irradiated[7] until *ca.* 25 ml CO (= 1 mmol) have been evolved, and then treated with spectroscopically pure *cis*-azobenzene (0.20 g, 1.1 mmol). After 0.5 h the solvent is removed; unreacted $Cr(CO)_6$ and azobenzene can be sublimed from the residue at 30 °C in a high vacuum. The crude product is recrystallized from THF/hexane at −78 °C and dried in a high vacuum. Yield 0.20 g (53 %), m.p. 62—65 °C.

trans-Azobenzene-bis(pentacarbonylchromium) (2)

After evolution of gas has ceased, the irradiated solution of $Cr(CO)_6$ (0.44 g, 2 mmol) in THF is treated with commercial azobenzene (0.18 g, 1 mmol). The solvent is removed and the residue dried in a high vacuum. The bluish violet crude product is dissolved at −45 °C in a small volume of THF; on addition of pentane at −78 °C, *(2)* crystallizes out. After repeated washing with pentane at −78 °C the complex is dried in a high vacuum at room temperature. Yield 0.14 g (25 %).

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CAS Registry numbers:
(1), 58448-96-7; *(2)*, 58448-97-8; *(3)*, 58448-98-9

[1] Transition Metal Complexes of N-Containing Ligands, Part 10. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 9: *M. Herberhold* and *W. Bernhagen*, Z. Naturforsch. *29b*, 801 (1974).

[2] *M. Kooti* and *J. F. Nixon*, J. Organometal. Chem. *76*, C29 (1974); *ibid. 105*, 217 (1976).

[3] Cf. a) *G. P. Khare, R. G. Little, J. T. Veal*, and *R. J. Doedens*, Inorg. Chem. *14*, 2475 (1975), and literature cited therein; b) *S. D. Ittel* and *J. A. Ibers*, *ibid. 14*, 1183 (1975), and literature cited therein.

[4] *G. Huttner, H.-G. Schmid, H. Willenberg*, and *Th. Stark*, J. Organometal. Chem. *94*, C 3 (1975).

[5] *E. O. Fischer, K. Öfele, H. Essler, W. Fröhlich, J. P. Mortensen*, and *W. Semmlinger*, Chem. Ber. *91*, 2763 (1958); *B. Nicholls* and *M. C. Whiting*, Proc. Chem. Soc. *1958*, 152; J. Chem. Soc. *1959*, 551.

[6] Elemental analyses gave correct values for all complexes. The molybdenum and tungsten compounds analogous to *(1)* and *(2)* have also been prepared.

[7] High-pressure mercury vapor lamp, original Hanau, Q 700.

μ-Bromo-μ-phenylmethylidynebis(tetracarbonylrhenium)[1]

By *Ernst Otto Fischer, Gottfried Huttner, Tassilo Lothar Lindner, Albin Frank*, and *Fritz Roland Kreissl*[*]

On reaction of phenylmethoxycarbenenonacarbonyldirhenium *(1)*[2] with aluminum bromide we observed expulsion of the CH_3O group, elimination of a CO molecule, and entry of a Br atom into the complex:

$$Re_2(CO)_9C(OCH_3)C_6H_5 + Al_2Br_6 \xrightarrow[-30\,^\circ C]{Toluene} Re_2(CO)_8(CC_6H_5)Br + CO + \{Al_2Br_5OCH_3\}$$
(1) *(2)*

Either the formation of a bromo- and a phenylcarbyne ligand with retention of the rhenium-rhenium bond or the linkage of two tetracarbonyl rhenium fragments *via* a bromo- and a phenylmethylidyne bridge appeared to account for the structure of the new compound *(2)*. X-Ray structure analysis

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Arcisstrasse 21, 8000 München 2 (Germany)

[956 independent reflections ("Syntex P21"); solution with "Syntex XTL" ($R_1 = 0.057$)] of the complex confirmed the second alternative, and especially the bridging C_6H_5C ligand having sp^2-hybridized carbon (cf. Fig. 1). Cell parameters: space group P21/c; $a = 1330.9$, $b = 1083.9$, $c = 1817.1$ pm; $\beta = 134.6°$; $V = 1866.1 \times 10^6$ pm^3; $Z = 4$; $d_{calc} = 2.725$ g cm^{-3}.

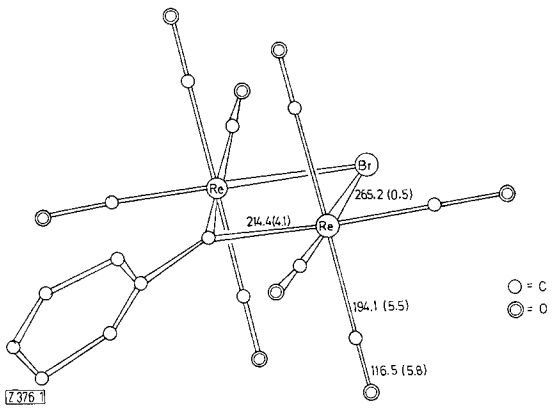

Fig. 1. Molecular structure of $Re_2(CO)_8(CC_6H_5)Br$ *(2)*.

The four-membered ReBrReC ring in *(2)* also differs from the MCMC rings found in the structures of the compounds bis(μ-trimethylsilylmethylidyne)tetrakis(trimethylsilylmethyl)-diniobium[3] and di-μ-ethoxycarbonylmethylidynebis(tetracarbonylmanganese)[4] in that the methylidyne bridge, discovered here to occur singly for the first time, between the two coordination centers contains a substituent devoid of a hetero atom. The Re—C bond length is 214.4 (4.1) pm, and is thus 14 pm shorter than a calculated Re—C single bond (covalent radii: Re = 151 pm[5], C = 77 pm). As expected, the Re—Br distance is longer than in Re_3Br_9 (254.3 pm, rhenium as Re^{3+}[6]); having a value of 265.2 (0.5) pm it corresponds to the sum of the single bond radii (Br = 114 pm). Both bridge atoms are located approximately in the plane of the equatorial carbonyl groups. The phenyl ring is twisted by 72° relative to this plane.

The results of total elemental analysis and IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectrometry are in accord with this finding.—In the IR spectrum (in *n*-hexane) of compound *(2)* four bands appear in the ν_{CO} frequency range at 2081 m, 2023 vs, 2013 s, and 1953 s cm^{-1}.—In the ^{1}H-NMR spectrum the phenyl protons are observed as two multiplets in the intensity ratio 3:2 at 7.50 and 6.84 ppm (in CD_2Cl_2, −20 °C, TMS as internal standard).—The proton noise decoupled ^{13}C-NMR spectrum (in CD_2Cl_2, −20 °C, relative to CD_2Cl_2 = 54.16 ppm) contains a total of seven signals: four in the carbonyl and three in the aromatic range. The signal at 201.20 ppm is assigned to the bridging carbon atom, the three signals at 186.85, 186.10, and 185.88 ppm to the carbonyl carbon atoms, and the remaining signals at 129.78, 127.84, 110.69 ppm to the phenyl carbon atoms.—In the mass spectrum the molecular peak appears at $m/e = 768$ (based on ^{187}Re and ^{81}Br, ion source TO 4, 50 eV).

Procedure:

All operations are to be performed under nitrogen with dried (Na, P_4O_{10}) and N_2-saturated solvents.—Compound *(1)* (1.00 g, 1.34 mmol) and Al_2Br_6 (0.72 g, 1.34 mmol) are stirred together in toluene (10 ml) at −30 °C for 30 min. Unconsumed Al_2Br_6 is decomposed at −70 °C with methanol and the solution decanted. Complex *(2)* in the residue is purified by chromatography in methylene chloride/pentane over silica gel and recrystallized from methylene chloride/diethyl ether: black crystals, decomposing above 108 °C; yield 0.5 g (49%).

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CAS Registry numbers:
$Re_2(CO)_9C(OCH_3)C_6H_5$: 38855-78-6; Al_2Br_6: 18898-34-5; $Re_2(CO)_8CC_6H_5Br$: 58384-14-8

[1] Transition metal carbene complexes, Part 87.—Part 86: *H. Brunner, J. Doppelberger, E. O. Fischer*, and *M. Lappus*, J. Organometal. Chem., in press.
[2] *E. O. Fischer, E. Offhaus, J. Müller*, and *D. Nöthe*, Chem. Ber. *105*, 3027 (1972).
[3] *F. Hug, W. Mowat, A. C. Skapski*, and *G. Wilkinson*, Chem. Commun. *1971*, 1477.
[4] *W. A. Herrmann*, Angew. Chem. *86*, 895 (1974); Angew. Chem. Int. Ed. Engl. *13*, 812 (1974).
[5] *N. I. Gapotchenko, N. V. Alekseev, N. E. Kolobova, K. N. Anisimov, I. A. Ronova*, and *A. A. Johansson*, J. Organometal. Chem. *35*, 319 (1972).
[6] *F. A. Cotton* and *S. J. Lippard*, Inorg. Chem. *4*, 59 (1965).

Mechanism of the Thermal Conversion of 3,3′-Bicyclopropenyls into Benzene Derivatives[**]

By *James H. Davis, Kenneth J. Shea*, and *Robert G. Bergman*[*]

Possible mechanisms for the highly exothermic ($\Delta H_0 = -120$ kcal/mol) thermal conversion of 3,3′-bicyclopropenyls [*e.g. (1)*] into benzene derivatives fall into two general groups[1]. The first (which we shall refer to here as group A) postulates some sort of initial bonding interaction between the two cyclopropenyl rings (examples are concerted double ring expansion, the classical Breslow[1a] prismane mechanism, and the recently suggested tricyclic diradical mechanism offered by *Weiss* and *Köbl*[1g]). The other group (B) involves cyclopropene ring bond cleavage as the initial critical step[2]. Both *Weiss* and *Köbl*[1g] and *de Wolf et al.*[1c] have recently reported that, in addition to aromatization, substituted bicyclopropenyls also undergo Cope rearrangement[3]. 3,3′-Dimethyl-3,3′-bicyclopropenyl *(1)*, for example, rearranges to diastereomers *(2)* and *(3)* in competition with its conversion into xylenes[1e]. During a recent chemiluminescence study[4] of the aromatization of *(1)*, we, too, observed its conversion into *(2)* and *(3)*. It occurred to us that the stereochemical relationship of these two molecules was such that an examination of their aromatization might allow us to decide between the mechanisms A and B discussed above, since pathways involving initial ring cleavage (B) destroy the stereochemical distinction between *(2)* and *(3)*.

We have therefore (i) found methods to preparatively separate *(2)* and *(3)* from *(1)* and xylene products, (ii) carried out chemical correlations to determine which of these diastereomers is the DL and which the *meso* form, and (iii) determined

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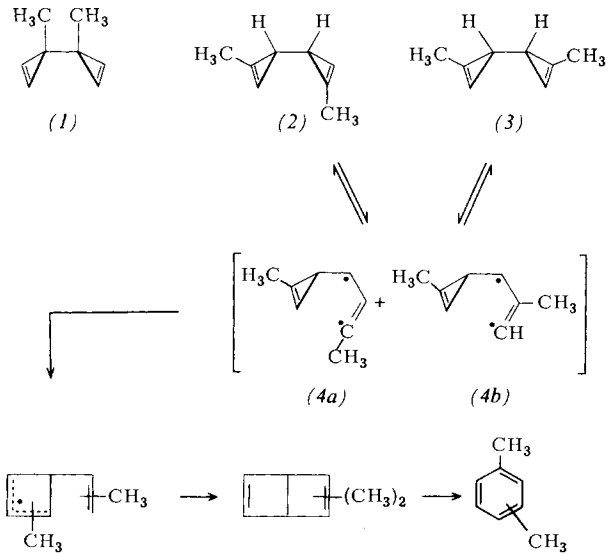

the zero-time (kinetic) ratio of xylenes formed from each diastereomer. Our results provide strong evidence for the ring-cleavage mechanism (group B).

Separation of *(2)* and *(3)* was achieved by preparative VPC at 25 °C on a 20′ × 1/4″ *glass* column packed with 30% SE-30 on chromosorb WAW (60/80). The stereochemistry of each diastereomer was determined by chemical correlation with DL- and *meso*-3,4-dimethyl-2,5-hexanediones, whose structures were assigned using chiral shift reagents[5a] and confirmed by asymmetric hydroboration of the DL-diketone[5b].

Pyrolysis of *(1)*, *(2)*, and *(3)*, in a 200-ml vessel made of lead-alkaline glass[6] (temperature range 160—200 °C), along with VPC analysis of *all three* xylenes at very low percentage conversion[7] provided information about both the Cope rearrangement and aromatization kinetic product distributions (Table 1). The chemical correlations confirmed earlier judg-

Table 1. Extrapolated zero-time xylene distributions formed in the gas phase pyrolysis [a] of dimethylbicyclopropenyls *(2)*, *(3)*, and *(1)* at 169.5 °C.

Compound	Xylene isomers [%]		
	p	*m*	*o*
(2) [b]	20±1	72±2	8±3
(3)	27±2	62±2	11±4
(1)	26±5	2±2	72±5

[a] Pyrolyses were carried out in a well-conditioned static system (see text) at a total pressure of *ca.* 150 torr (15 torr of substrate and 135 torr of pentane as bath gas). Samples were vaporized into the reaction vessel and removed using a conventional vacuum line system connected to the vessel. [b] Extrapolated from VPC data (see ref. [7]) taken at 4 points ranging from reaction times of 300 s (6.4% loss of starting material: 0.86% conversion to xylenes) to 1000 s (23.5% conversion of starting material, 1.50% conversion to xylenes). Data for *(3)* and *(1)* were taken over similar reaction times.

ments[1e,f] that the Cope process favors the chair transition state. The *(2)*/*(3)* ratio extrapolated to zero time (130±10) showed *no* variation with temperature[1e] and is very similar to that observed in acyclic systems[8] (one therefore needs no "special geometric and bonding effects"[1e] to account for it)[9]. Pyrolysis of isolated *(2)* and *(3)* (92% and 95% pure, respectively) demonstrated (i) that the diastereomers interconvert under the reaction conditions (by a pathway different from one involving reconversion into *(1)*) at rates (cf. Table 2) competitive with xylene formation, and (ii) the zero-time (kinetic) distributions of *o*-, *m*- and *p*-xylene formed from each diastereomer are very similar.

Table 2. Rate constants [a] (in s^{-1}, $\times 10^5$) for interconversion of bicyclopropenyls *(1)*, *(2)*, and *(3)* and for their conversion into xylenes.

Starting material \ Product	*(2)*	*(3)*	Xylenes [b]
(1)	18±2	0.14±0.02	3.6±1.0
(2)	—	25 ±2	1.7±0.5
(3)	25±2	—	1.9±0.5

[a] Determined by computer simulation of concentration-*vs.*-time curves (at both low and extensive conversion for *(1)*, *(2)*, *(3)* and total xylenes), using the MSIM4 program written by Ms. *Frances Houle* in collaboration with Professor *D. L. Bunker* at the University of California, Irvine. We are grateful to Ms. *Houle* and Professor *Bunker* for providing us with a copy of the program.
[b] Summation rate constants for appearance of all xylenes. For individual (relative) rates of formation, see Table 1.

The data are clearly inconsistent with group A mechanisms[1a, 1g], since these should give dramatically different xylene distributions from diastereomers *(2)* and *(3)*. Initial (reversible) ring opening to diradicals *(4a)* and *(4b)* (or their vinylcarbene relatives[2]), however, nicely accounts for both the similarity of product distributions from *(2)* and *(3)* and for the competitive interconversion of these compounds, if one assumes that the relative rates of formation of *(4a)* and *(4b)* from *(2)* and *(3)* are very slightly different. This mechanism also accounts for the fact that the percentage of *m*-xylene formed directly from *(1)* at "zero time" is zero within experimental error. These results, taken together with the recent observation that Dewar benzenes are required intermediates in the aromatization[4], lead us to the overall mechanism outlined. We suggest that ring opening to diradicals (or carbenes) *(4)* followed by cyclopropenylmethyl ring expansion[10, 11], closure to Dewar benzenes, and subsequent concerted[12] ring opening of these intermediates, is the aromatization mechanism most consistent with presently available experimental evidence.

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CAS Registry numbers:
(1), 31707-64-9; *(2)*, 58374-90-6; *(3)*, 55930-24-0; *p*-xylene, 106-44-5; *m*-xylene, 108-39-4; *o*-xylene, 95-48-7

[1] a) *R. Breslow, P. Gal, H.-W. Chang*, and *L. J. Altman*, J. Am. Chem. Soc. *87*, 5139 (1965); b) *R. Weiss* and *H. P. Kempcke*, Tetrahedron Lett. *1974*, 155; c) *R. Weiss* and *S. Andrae*, Angew. Chem. *85*, 145, 147 (1973); Angew. Chem. Int. Ed. Engl. *12*, 150, 152 (1973); d) *W. H. de Wolf, W. Stol, I. J. Landheer*, and *F. Bickelhaupt*, Rec. Trav. Chim. Pays-Bas *90*, 405 (1971); e) *W. H. de Wolf, I. J. Landheer*, and *F. Bickelhaupt*, Tetrahedron Lett. *1975*, 179; f) *R. Weiss* and *H. Köbl*, J. Am. Chem. Soc. *97*, 3222 (1975); g) *97*, 3224 (1975).
[2] *E. J. York, W. Dittmar, J. R. Stevenson*, and *R. G. Bergman*, J. Am. Chem. Soc. *94*, 2882 (1972); *95*, 5681 (1973).
[3] See ref. [1a] and a) *L. T. Scott* and *M. Jones, Jr.*, Chem. Rev. *72*, 181 (1972); b) *A. T. Balaban*, Rev. Roum. Chim. *17*, 883 (1972).
[4] *N. J. Turro, G. B. Schuster, R. G. Bergman, K. J. Shea*, and *J. H. Davis*, J. Am. Chem. Soc. *97*, 4758 (1975).
[5] a) *M. Kainosho, K. Ajisaka, W. H. Pirkle*, and *S. D. Bears*, J. Am. Chem. Soc. *94*, 5924 (1972); b) *H. C. Brown, N. R. Ayyangar*, and *G. Zweifel, ibid. 86*, 397 (1964). The early-eluting bicyclopropenyl diastereomer proved to be DL-*(2)*.
[6] *G. Beasley*, Ph. D. Dissertation, Yale University 1970.
[7] VPC resolution of the three xylenes required the use (with temperature programming) of an "internal tandem" 20′ × 1/4″ glass column packed with 15′ of 30% SE-30 on chromosorb WAW (60/80) followed by 5′ of 5% DC-555 and 5% Bentone-34 on chromosorb WAW (60/80).
[8] *W. von E. Doering* and *W. R. Roth*, Tetrahedron *18*, 67 (1962); b) *M. J. Goldstein* and *M. S. Benzon*, J. Am. Chem. Soc. *94*, 7147 (1972); c) *M. J. Goldstein* and *M. R. DeCamp, ibid. 96*, 7356 (1974).
[9] Because of the unusual symmetry of *(1)*, the chair and boat transition states may be interconverted by a simple rotation rather than a ring flip, and the rigidity of the system prevents rearrangement by a number of other conformations available to the more flexible acyclic system [8b, c].

It therefore seems likely that the *(1)*→*(2)* and *(1)*→*(3)* $\Delta\Delta F^{\neq}$ of 4.3 kcal/mol (166 °C) reflects the true chair-boat transition state free energy difference for this system.

[10] This pathway is analogous to the ionic mechanism suggested by *Weiss et al.* [1b, 1c] for the silver-catalyzed conversion of bicyclopropenyls to Dewar benzenes, except that due to the extreme difficulty of generating charge-separated species in the gas phase, neutral diradicals rather than ionic intermediates are probably involved here; see, for example, a) *L. Salem* and *C. Rowland*, Angew. Chem. *84*, 86 (1972); Angew. Chem. Int. Ed. Engl. *11*, 92 (1972); b) *E. F. Hayes* and *A. K. Q. Siu*, J. Am. Chem. Soc. *93*, 2090 (1971); c) *L. Salem* and *W.-D. Stohrer*, to be published; d) *W. A. Goddard* and *J. H. Davis*, unpublished results.

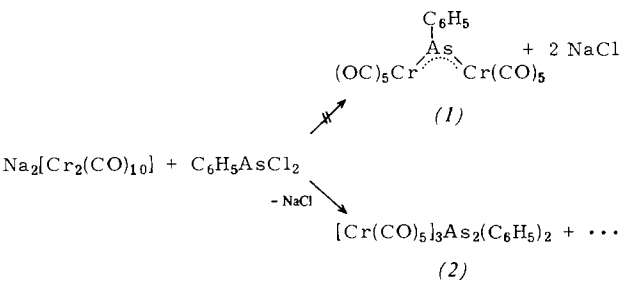
[11] Interestingly, we have been unable to find a study in the literature of cyclopropenylcarbinyl radicals to use as a model for the ring expansion of *(4a)* and *(4b)*. It seems likely, however, that the strain relief and incipient allylic delocalization generated in the transition state for such an expansion would render it an extremely facile process.

[12] *R. Breslow, J. Napierski*, and *A. H. Schmidt*, J. Am. Chem. Soc. *94*, 5906 (1972).

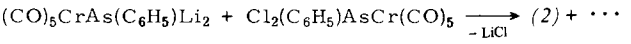
"Arsenobenzene", C_6H_5—As=As—C_6H_5, as a Bridging μ_3 Ligand in a Transition Metal Complex[**]

By *Gottfried Huttner, Hans-Georg Schmid, Albin Frank*, and *Olli Orama*[*]

In an attempt to synthesize the arsinidene complex *(1)*[1], according to:



we surprisingly isolated not *(1)* but instead the red complex *(2)*, m.p. 142 °C (dec.), among other hitherto unidentified products. The new compound *(2)* can also be prepared[2] according to:



The molecular ion of *(2)* does not appear in its mass spectrum; however, intense peaks are observed for the fragment ions $Ph_2As_2Cr(CO)_5$ (m/e = 496) and Ph_2As_2 (m/e = 304). The IR spectrum exhibits absorptions which are characteristic of phenyl groups; the band pattern in the ν_{CO} region indicates the presence of several differently coordinated $Cr(CO)_5$ units. The ^{1}H-NMR spectrum (solution in CD_2Cl_2) only shows signals due to phenyl protons.

X-Ray structure analysis[3] shows that arsenobenzene, Ph—As=As—Ph, which is homologous to azobenzene, is stabilized as a ligand in the complex *(2)*. The two arsenic atoms both form coordinative bonds to $Cr(CO)_5$ groups. In addition, the As=As double bond participates in π-interaction with a third $Cr(CO)_5$ group (cf. Fig. 1).

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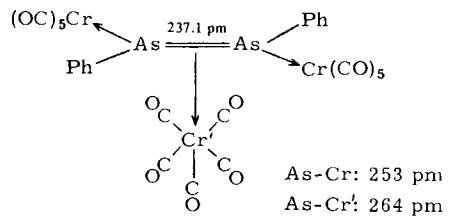

Fig. 1. Molecular structure of the arsenobenzene complex *(2)*.

In the only example of a R_2As_2 complex yet known, $(OC)_4Fe(C_6F_5As)_2$[4], the ligand is merely stabilized by π addition to a carbonylmetal fragment.

Evidence supporting formulation of the complex *(2)* with an As=As double bond is provided by the arsenic-arsenic interatomic distance (Fig. 1), which is 9 pm shorter than the As—As single bond in $C_5H_5(CO)_2Mn\{PhHAs\}_2Mn(CO)_2C_5H_5$ (246 pm)[5], in spite of the elongation due to coordination.

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CAS Registry numbers:
$Na_2[Cr_2(CO)_{10}]$, 15616-67-8; $C_6H_5AsCl_2$, 696-28-6; $(OC)_5CrAs(C_6H_5)Li_2$, 55590-59-5; $Cl_2(C_6H_5)AsCr(CO)_5$, 58448-94-5; $[Cr(CO)_5]_3As_2(C_6H_5)_2$, 58448-95-6

[1] *G. Huttner* and *H.-G. Schmid*, Angew. Chem. *87*, 454 (1975); Angew. Chem. Int. Ed. Engl. *14*, 433 (1975).

[2] *G. Huttner* and *H. G. Schmid*, to be published.

[3] 1157 diffractometer data ("Syntex P21"); solution with "Syntex XTL" (R_1 = 0.06).

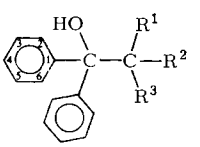
[4] *P. S. Elmes, P. Leverett*, and *B. O. West*, Chem. Commun. *1971*, 747.

[5] *G. Huttner, H.-G. Schmid* and *H. Lorenz*, unpublished.

Magnetic Nonequivalence of the C Atoms of Prochiral Diphenylmethyl Groups in ^{13}C-NMR Spectroscopy

By *Hans Otto Kalinowski, Bernd Renger*, and *Dieter Seebach*[*]

The magnetic nonequivalence of diastereotopic groups manifested in ^{1}H-NMR spectra has proved to be of value in the elucidation of stereochemical problems[1]. Only very few comparable studies have so far been performed in ^{13}C-NMR spectroscopy[2–4]. We here report the magnetic nonequivalence of the C atoms of diastereotopic phenyl groups in tertiary alcohols of type *(1)*[5].



(1a-h)

Table 1 shows the chemical shift differences of the ^{13}C-NMR signals of the phenyl carbon atoms of these compounds. The relatively large difference of the signals for the ring C^1 atoms is not surprising since these atoms are located closest to the center of chirality (except in the case of *(1i)*); the magnitude of the difference remains practically constant within the classes of compounds *(1a–c)* and *(1d–h)*. The largest splittings are observed for the carbonyl-containing compounds *(1a–c)*, in which effective hydrogen bonding could be responsible for

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Table 1. Chemical shift difference Δδ of the ^{13}C-NMR signals of the ring carbon atoms in *(1)* (*ca.* 1 M solution in $CDCl_3$; 30°C) [a].

	Compound *(1)*			Signals of C^1	Δδ [ppm]			
	R^1	R^2	R^3	[ppm]	C^1	C^2, C^6	C^3, C^5	C^4
(a)	H	C_2H_5	$COOCH_3$	147.6 144.5	3.1	—	—	0.3
(b)	H	CH_3	$CON(CH_3)_2$	148.6 145.2	3.4	0.4	—	0.1
				148.9 [b] 145.5	3.4 [b]	0.3 [b]	—	—
(c)	H	CH_3	$COOC_2H_5$	147.8 144.7	3.1	0.1	—	0.2
(d)	H	—NH—$(CH_2)_4$—		146.6 144.4	2.2	0.6	0.5	0.8
(e)	H	—NH—$CH(CH_3)$—$(CH_2)_3$—		146.6 144.5	2.1	0.5	0.5	0.3
(f)	H	—NH—$(CH_2)_2$—$CH(CH_3)$—CH_2—		146.0 143.8	2.2	0.5	0.3	0.5
(g)	H	—NH—$(CH_2)_3$—$CH(CH_3)$—		147.4 145.0	2.4	0.7	—	0.3
(h)	H	—NH—$(CH_2)_3$—		148.3 145.5	2.8	0.3	0.3	—
(i)	H	$-\overset{\oplus}{N}H_2-(CH_2)_3-$ $Cl^{\ominus}$		145.0 [c] 144.6	0.4	0.7	0.3	0.3
(j)	H	SCH_3	C_6H_5	145.9 144.7	1.2	>0.1 [d]	>0.1 [d]	0.1

[a] The spectra were recorded with a CFT 20 Varian instrument (8K store, accuracy: 0.05 ppm).
[b] In dimethyl sulfoxide as solvent (to rupture the H bonds: cf. ref. [6]); dilution of the solution has no effect on the splitting and chemical shift of the signals.
[c] In dimethyl sulfoxide as solvent.
[d] In the phenyl region there are 12 signals of which only those for C^1 and C^4 can be unequivocally assigned. The splitting of the signals for C^2, C^6 and C^3, C^5 is in any case greater than 0.1 ppm since the lines are separated from each other by more than 0.1 ppm.

preference of a particular conformer (see Table 1, b). Comparison of the chemical shift differences observed for the signals of atoms C^2 and C^6, C^3 and C^5 and C^4, shows that, although significantly smaller than for C^1 except in the case of *(1i)*, they do not decrease with increasing distance from the center of chirality, as is claimed in the literature[1,2]. Instead, the magnitude of the difference alternates or (in one case) is observable only for the atom C^4. No explanation of this finding can yet be given. While there does seem to be a relationship between the magnitude of the chemical shift difference (compound *(1b,c,f,g)*) and the inductive and mesomeric substituent effect—the C atoms in positions 3 and 5 seem to be the least affected—this explanation appears unsatisfactory in view of the similarity of the compounds.

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CAS Registry numbers:
(1a). 58473-61-3: *(1b)*. 20428-72-2: *(1c)*. 58473-62-4:
(1d). 467-60-7: *(1e)*. 58473-63-5: *(1f)*. 58473-64-6:
(1g). 58473-65-7: *(1j)*. 52791-94-3

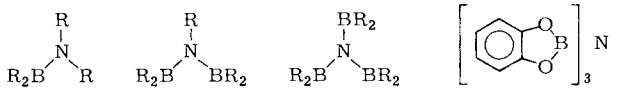
[1] *W. B. Jennings*, Chem. Rev. *75*, 307 (1975).
[2] *J. I. Kroschwitz, M. Winokur, H. J. Reich*, and *J. D. Roberts*, J. Am. Chem. Soc. *91*, 5927 (1969).
[3] *J. Dabrowski et al.*, Org. Magn. Reson. *4*, 131, 137, 443 (1973); *5*, 483 (1973); *D. Dodrell* and *N. V. Riggs*, Aust. J. Chem. *25*, 2715 (1972).
[4] *P. E. Rakita* and *R. Wright*, Inorg. Nucl. Chem. Lett. *11*, 47 (1975), first reported the magnetic nonequivalence of diastereotopic phenyl groups in a diphenylsilyl compound.
[5] Compounds *(1a–c)* were prepared at this institute in connection with the projected doctoral thesis of *W. Langer*.—*(1d–g)*: *B. Renger*, projected thesis; *D. Seebach* and *D. Enders*, Angew. Chem. *87*, 1 (1975); Angew. Chem. Int. Ed. Engl. *14*, 15 (1975).—*(1h,i)*: *D. Enders, B. Renger*, and *D. Seebach*, to be published.—*(1j)*: *D. Seebach* and *K. H. Geiss*, Angew. Chem. *86*, 202 (1974); Angew. Chem. Int. Ed. Engl. *13*, 202 (1974).—Satisfactory elemental analyses and spectroscopic data are available for all compounds.—Other α-substituted diphenylmethanols which contain no center of chirality in the molcule do not display any signal splitting for the geminal phenyl groups in the ^{13}C-NMR spectrum.
[6] *H. Kessler* and *M. Branik*, Tetrahedron *30*, 781 (1974).

Tris(3-methylborolan-1-yl)amine, an Electron-Deficient Triborylamine

By *Wolfgang Storch* and *Heinrich Nöth*[*]

Dedicated to Professor J. Goubeau on the occasion of his 75th birthday

Alkyl-substituted borylamines *(1)* are stable, whereas diborylamines *(2)* readily decompose with elimination of BR_3[1] and tris(diorganylboryl)amines *(3)* were hitherto unknown[2].



(1) *(2)* *(3)* *(4)*

Existence of the predicted $N(BF_2)_3$ with D_{3h} symmetry[3a] has so far not been demonstrated experimentally[3b]. The B_3N skeletal unit of a triborylamine can be synthesized, however, if the boron atoms have substituents capable of π back-bonding and if 1,3 nucleophilic rearrangement is impeded by incorporation in a ring system[4]; the *electron-rich* compound *(4)* may be cited as example[4a]. Above 150°C the latter mentioned stabilization effect raises the decomposition threshold in bis(borolan-1-yl)amines compared to $[(CH_3)_2B]_2NCH_3$ to over 150°C[5]. This has now made it possible to synthesize also the *electron-deficient* triborylamine *(9)* of type *(3)* in accordance with Equation (a), where exact control of stoichiometry and temperature permits stepwise replacement of the $(CH_3)_3Sn$ groups of *(5)* by the 3-methylborolanyl group.

The higher temperature and longer reaction time required on progressive removal of $(CH_3)_3Sn$ groups reflects the expected decrease in basicity of the nitrogen in the series *(5)*—*(9)*.

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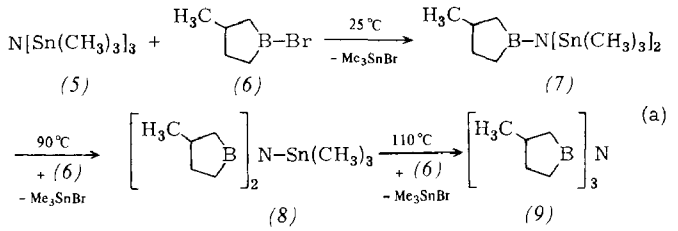
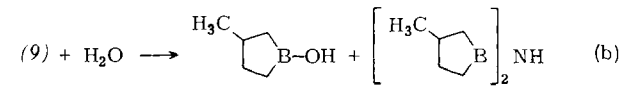


The products *(7)*—*(9)* were characterized by elemental analysis and NMR, IR, and MS spectra. *(9)* slowly decomposes at 180°C. Traces of moisture lead to rapid reaction in accordance with Eq. (b). Compounds *(7)* and *(8)* are also sensitive to hydrolysis and oxidation.



The NMR data of the 3-methylborolan-1-ylamines *(7)*, *(8)*, and *(9)* [δ^{11}B: −59.2, −64.0, and −67.8 ppm, resp.; δ^{14}N: 286, 228, and 206 ppm, resp.][6] confirm the coordination number 3 for the B and N atoms. In spite of the electropositive character of the boron, the borolanyl group withdraws electron density from the N atom through BN π interactions, recognizable by the downfield shift of the ^{14}N-NMR signal and by the ^{1}H-NMR signal of the $(CH_3)_3Sn$ group [δ^{1}H: −0.16 *(5)*, −0.26 *(7)*, and −0.35 ppm *(8)*].

Because of the low π-electron density on the three boron atoms and the lability of the B—N bonds, *(9)* is a powerful boronating reagent[7].

Tris(3-methylborolan-1-yl)amine (9)

A solution of 1-bromo-3-methylborolane *(6)* (5 ml; 6.0 g, 37.2 mmol) in toluene (15 ml) is added dropwise at −20°C to a stirred solution of tris(trimethylstannyl)amine *(5)* (6.25 g, 12.4 mmol) in toluene (20 ml). The mixture is allowed to warm up slowly and then heated under reflux for 7 h. Fractional distillation (10 cm silver-mantle Vigreux column) of the residue remaining after removal of volatiles affords 8.4 g Me_3SnBr (93%; b.p. 28—30°C/10^{-2} torr) and 2.6 g *(9)* (81%; b.p. 73—74°C/10^{-2} torr). *(9)* is a water-clear, viscous liquid which is very sensitive toward hydrolysis and oxidation.

Analogous reactions of *(5)* with *(6)* in toluene under modified conditions [molar ratios 1:2 and 1:1, resp.; reaction at 90°C (4 h) and room temperature (2 h), resp.] afford the trimethylstannyl(3-methylborolan-1-yl)amines *(8)* (78%; b.p. 89—91°C/10^{-2} torr) and *(7)* (75%; b.p. 117—119°C/10^{-1} torr).

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CAS Registry numbers:
(5), 1068-70-8; *(6)*, 22086-42-6; *(7)*, 58485-83-9; *(8)*, 58485-84-0; *(9)*, 58485-85-1

[1] Gmelins Handbuch der Anorganischen Chemie. Supplement to 8th Edit., Vol. 22: Borverbindungen, Part 4 (1975); *H. Nöth* and *H. Vahrenkamp*, J. Organometal. Chem. *16*, 357 (1969).

[2] ^{1}H-NMR data for the reaction products of $(CH_3)_2BBr$ and $(CH_3)_2BN[Si(CH_3)_3]_2$ indicate, *inter alia*, unstable $[(CH_3)_2B]_3N$; *H. Vahrenkamp*, Dissertation, Universität München 1967.

[3] a) *A. D. Buckingham*, Proc. Chem. Soc. London *1962*, 351; b) *R. G. Geanangel*, J. Inorg. Nucl. Chem. *32*, 3697 (1970).

[4] a) *M. F. Lappert* and *G. Srivastava*, Proc. Chem. Soc. London *1964*, 120; b) *H. Nöth* and *W. Regnet*, Z. Anorg. Allg. Chem. *352*, 1 (1967); *D. Nölle*, *H. Nöth*, and *W. Winterstein*, *ibid. 406*, 235 (1974).

[5] *R. Köster* and *D. Iwasaki*, Adv. Chem. Ser. *42*, 148 (1964); *H. Nöth* and *W. Storch*, Chem. Ber. *109*, 884 (1976).

[6] Values referred to the external standard $BF_3 \cdot O(C_2H_5)_2$ and saturated aqueous $NaNO_3$ solution.

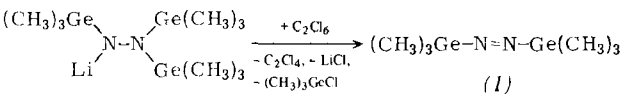
[7] *H. Nöth* and *W. Storch*, unpublished.

Bis(trimethylgermyl)diimine[1]

By *Nils Wiberg*, *Sham Kumar Vasisht*, and *Gerd Fischer*[*]

Bis(silyl)diimines (azosilanes) corresponding to the bis(alkyl)diimines (azoalkanes) have been known for several years[2]. However, all attempts to synthesize higher homologs of the type X—N=N—X (X = GeR_3, SnR_3, or PbR_3) have so far remained without success[3].

Adaptation of the oxidation of *N*-lithium tris(trimethylsilyl)-hydrazide[2], which affords bis(trimethylsilyl)diimine, to the preparation of bis(trimethylgermyl)diimine *(1)* was initially unsuccessful since the germyl hydrazide was not oxidized to *(1)* but further to nitrogen. However, in hexachloroethane we have now found an oxidizing agent providing access to the very easily oxidized azogermane *(1)* according to:



(Preparation of an azostannane—probably even more sensitive to oxidation—accordingly appears extremely difficult.)

The blue diimine derivative *(1)*, which can be sublimed at −45°C *in vacuo* (10^{-4} torr), expectedly gives only one signal in its ^{1}H-NMR spectrum ($\delta = -21.8$ Hz, TMS as internal standard, in C_6H_6). According to mass spectrometric studies the energy required for ionization of the highest occupied n_+ orbital of the nitrogen lone pairs is only 5.95 ± 0.05 eV; it is thus lower than the ionization energy of bis(trimethylsilyl)-diimine and much lower than that of bis(trimethylmethyl)diimine (cf. Fig. 1). The absorption maximum for the $n_+ \rightarrow \pi^*$ electronic transition responsible for the color of *(1)* on the other hand lies at 14310 cm^{-1} between the corresponding absorption maxima of the carbon and the silicon compound. This finding can be rationalized in a simplified manner in terms of inductive and—especially with regard to the π* orbital—mesomeric effects of the substituents attached to the azo group[4].

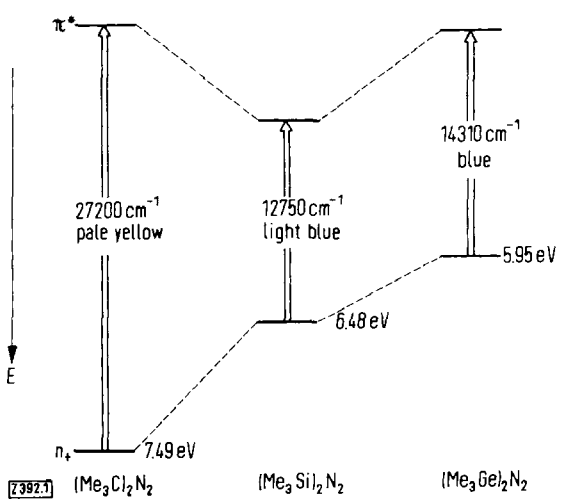


Fig. 1. Ionization energies of the n_+ orbital and wave numbers of the electronic transition between the highest occupied n_+ and the lowest unoccupied π* orbital of diimines $(CH_3)_3E—N=N—E(CH_3)_3$ (E = C, Si, Ge).

The azogermane *(1)*, which is readily hydrolyzed and extremely sensitive to oxygen[5], has a thermal instability resem-

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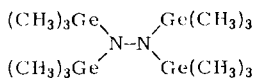
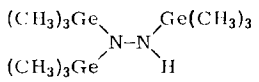
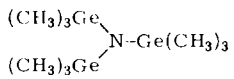
bling that of the corresponding azosilane (thermolysis occurring above *ca.* −35 °C). In analogy with $(Me_3Si)_2N_2$[6a] and $Me_3SiN_2GeMe_3$[6b], it decomposes at low temperatures almost exclusively *via* disproportionation to nitrogen and tetrakis(trimethylgermyl)hydrazine *(2)*, which is also accessible by another route[7]. At higher temperatures, increasing amounts of *(3)*–*(6)* and hexamethyldigermane *(7)*[8] are also formed.



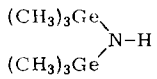
(2)



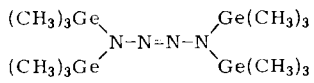
(3)



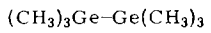
(4)



(5)



(6)



(7)

The yields of thermolysis products of *(1)* obtained at 80 °C in pentane, *e.g.*, amount to (the values in parentheses refer to the corresponding compound with Si in place of Ge): 50 (20)% *(2)*, 10 (25)% *(3)*, 10 (25)% *(4)*, 1 (10)% *(5)*, 20 (20)% *(6)*, 10 (0)% *(7)*.

Procedure:

A solution of hexachloroethane (6.0 mmol) in ether (50 ml) is added dropwise over 1 h to a stirred solution of *N*-lithium tris(trimethylgermyl)hydrazide[7] (10.0 mmol) in ether (100 ml) at −70 °C. After a reaction time of 1 h the solvent and trimethylgermyl chloride are removed as quickly as possible in the temperature range −70 to −50 °C and the product *(1)*, which volatilizes between −45 and −35 °C at 10^{-4} torr, is condensed in a cold trap at −60 °C (tetrachloroethane is not retained under these conditions). Repetition of this condensation affords *ca.* 2.0 mmol of pure *(1)*. All operations must be performed with rigorous exclusion of oxygen and moisture!

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CAS Registry numbers:
(1). 58485-86-2: *(2)*. 34478-38-1: *(3)*. 34478-49-4: *(4)*. 13361-68-7: *(5)*. 41990-70-9: *(6)*. 58485-87-3: *(7)*. 993-52-2: $(CH_3)_3CNNC(CH_3)_3$. 927-83-3: $(CH_3)_3SiNNSi(CH_3)_3$. 13436-03-8: *N*-lithium tris(trimethylgermyl)hydrazide. 58485-88-4: hexachloroethane. 67-72-1

[1] Part 19 of Diimine and Its Derivatives. This work was supported by an Alexander von Humboldt Grant to *S. K. V.*—Part 18: ref. [4]. Also Part 37 of Compounds of Silicon and Its Group Homologs.—Part 36: ref. [3c].

[2] *N. Wiberg. W.-Ch. Joo.* and *W. Uhlenbrock.* Angew. Chem. *80*. 661 (1968): Angew. Chem. Int. Ed. Engl. *7*, 640 (1968); *N. Wiberg, ibid. 83*, 379 (1971) and *10*, 374 (1971), respectively.

[3] Azo compounds of the type X—N=N—Y are already known: a) X = CR_3, Y = SiR_3: *U. Wannagat* and *C. Krüger*, Z. Anorg. Allg. Chem. *326*, 288 (1964); b) X = CR_3, Y = GeR_3: *N. Wiberg* and *M. Veith*, Chem. Ber. *104*, 3191 (1971); c) X = SiR_3, Y = GeR_3: *N. Wiberg, S. K. Vasisht, G. Fischer*, and *E. Weinberg, ibid. 109*, 710 (1976).

[4] *H. Bock, K. Wittel, M. Veith*, and *N. Wiberg*, J. Am. Chem. Soc. *98*, 109 (1976). —Thus the absorption of an azostannane is to be expected at higher wave numbers than in the case of *(1)*.

[5] Formation of $Me_3Ge—O—O—GeMe_3$.

[6] a) *N. Wiberg* and *W. Uhlenbrock*, J. Organometal. Chem. *70*, 239, 249 (1974); b) apart form nitrogen the diimine derivative affords only the asymmetric hydrazine derivative $(Me_3Si)_2N—N(GeMe_3)_2$.

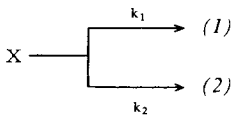
[7] *N. Wiberg* and *M. Veith*, Chem. Ber. *104*, 3176 (1971).

[8] Hexamethylazostannane should therefore already decompose preferentially to nitrogen and hexamethyldistannane.

Use of the Isoselectivity Principle for Distinguishing Cationic π- and σ Complexes[**]

By *Bernd Giese* and *Joachim Stellmach*[*]

Use of the kinetic selectivity principle which postulates a relationship between the competition constants $\varkappa$ and the structures of intermediates X has become subject to increasing criticism[1]. We were recently able to show that the differences in activation enthalpies $\Delta H_2^{\ddagger} - \Delta H_1^{\ddagger}$ determined from the temperature dependence of $\varkappa$ provide a much better description of intermediates[2].



$$\varkappa = k_1/k_2$$

$$\log\frac{k_1}{k_2} = \frac{\Delta H_2^{\ddagger} - \Delta H_1^{\ddagger}}{2.303 \cdot R \cdot T} - \frac{\Delta S_2^{\ddagger} - \Delta S_1^{\ddagger}}{2.303 \cdot R}$$

As a result of that work we derived the isoselective relationship as a new criterion for distinguishing between intermediates[2].

$$\delta(\Delta H_2^{\ddagger} - \Delta H_1^{\ddagger}) = T_{is} \cdot \delta(\Delta S_2^{\ddagger} - \Delta S_1^{\ddagger}) \qquad \text{(a)}$$

The subscripts 1 and 2 stand for the competing trapping reactions of X leading to the compounds *(1)* and *(2)*, respectively. The symbol δ indicates that only the changes in the activation parameters occurring on structural variation of X are related to each other.

The first application of the isoselectivity principle to radical halogen abstraction permitted a distinction to be made between π- and σ radicals[2]. In order to examine the general significance and scope of equation (a) we have now applied it to the ionic intermediates occurring on electrophilic additions to olefins. We have recently deduced that addition of halogens and benzenesulfenyl chloride to dimethyl norbornenedicarboxylate *(3)* involves intermediate formation of the π complexes *(4)* to *(6)*, *i.e.* bridged ions with electron deficient bonds, and complexes *(7)*, *i.e.* bridged onium ions without electron-deficient bonds[3,4]. Intramolecular *endo* attack of the ester groups on the carbon atoms C-6 and C-5 leads to the lactone esters *(8)* to *(15)*. The isomer ratios of *(8)*/*(12)* to *(11)*/*(15)* correspond to the selectivity values k_6/k_5 because the mixtures of isomers are formed in kinetically controlled reactions[5].

According to equation (b), which is obtained by subtraction of two Eyring relationships, the temperature dependence of the selectivity values k_6/k_5 yields the differences in activation

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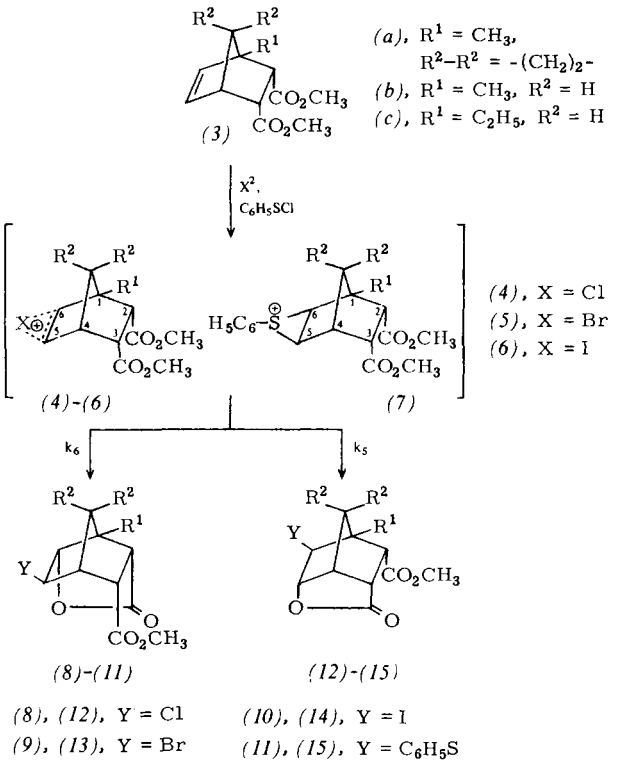

enthalpies $\Delta H_5^{\ddagger} - \Delta H_6^{\ddagger}$ and the entropies of activation $\Delta S_5^{\ddagger} - \Delta S_6^{\ddagger}$ for the competing *endo* attack at C-5 and C-6 of the intermediates *(4)* to *(7)*.

$$\log \frac{k_6}{k_5} = \frac{\Delta H_5^{\ddagger} - \Delta H_6^{\ddagger}}{2.303 \cdot R \cdot T} - \frac{\Delta S_5^{\ddagger} - \Delta S_6^{\ddagger}}{2.303 \cdot R} \qquad \text{(b)}$$

Measurements performed in chloroform from -60 to $+60$°C exhibit an average error of $\pm 10\%$ in the activation enthalpies and ± 0.3 e.u. in the entropies of activation[6].

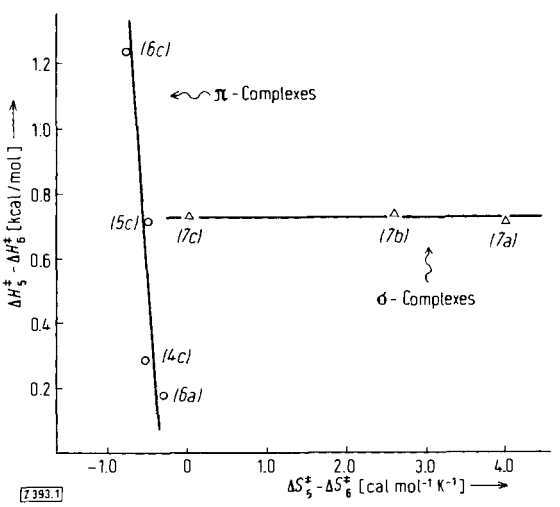

Fig. 1. Relationship between the activation parameters for competing attack of the ester on C-5 and C-6 of the intermediates *(4)* to *(7)* in chloroform.

Plotting the activation parameters gives one straight line for the halogen-bridged and another for the sulfur-bridged intermediates of electrophilic additions to *(3)* (Fig. 1). Their slopes correspond to the proportionality factors T_{is}. These are almost infinity for the halogen-containing intermediates *(4)* to *(6)* and zero for the intermediate *(7)*. Thus variations in the halogen-containing intermediates *(4)* to *(6)* predominantly affect the differences in activation enthalpies $\Delta H_5^{\ddagger} - \Delta H_6^{\ddagger}$, while changes in the intermediate *(7)* are reflected only in the differences in the entropies of activation $\Delta S_5^{\ddagger} - \Delta S_6^{\ddagger}$. These differences demonstrate that addition of halogen to *(3)* involves a different type of intermediate from that occurring in the addition of benzenesulfenyl chloride.

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CAS Registry numbers:
(3a). 52356-23-7; *(3b)*: 52356-25-9; *(3c)*. 52356-29-3; *(4a)*. 58486-19-4; *(4b)*. 58486-20-7; *(4c)*. 58486-21-8; *(5a)*. 58486-22-9; *(5b)*. 58486-23-0; *(5c)*. 58486-24-1; *(6a)*. 58486-25-2; *(6b)*. 58486-26-3; *(6c)*. 58486-27-4; *(7a)*. 58486-28-5; *(7b)*. 58486-29-6; *(7c)*. 58486-30-9; *(8a)*. 57199-29-8; *(8b)*. 58580-15-7; *(8c)*. 58580-16-8; *(9a)*. 52356-34-0; *(9b)*. 52356-35-1; *(9c)*. 52356-37-3; *(10a)*. 58580-17-9; *(10b)*. 58580-18-0; *(10c)*. 58580-19-1; *(11a)*. 57199-51-6; *(11b)*. 58580-20-4; *(11c)*. 58580-21-5; *(12a)*. 58580-22-6; *(12b)*. 57199-65-2; *(12c)*. 58580-23-7; *(13a)*. 52356-42-0; *(13b)*. 52356-43-1; *(13c)*. 52356-45-3; *(14a)*. 58580-24-8; *(14b)*. 57199-08-3; *(14c)*. 58580-25-9; *(15a)*. 57199-81-2; *(15b)*. 57199-11-8; *(15c)*. 58580-26-0; benzenesulfenyl chloride. 931-59-9

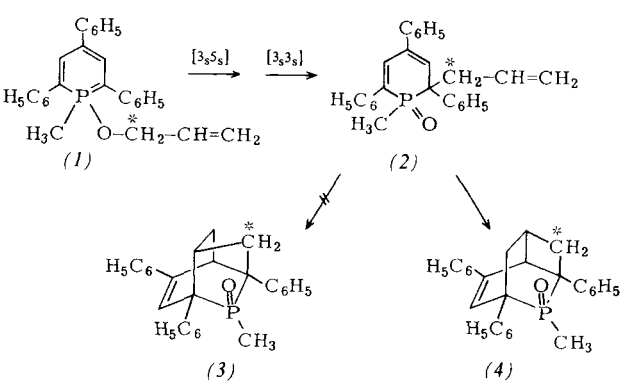
[1] *C. D. Johnson*, Chem. Rev. *75*, 755 (1975).
[2] *B. Giese*, Angew. Chem. *88*, 161 (1976); Angew. Chem. Int. Ed. Engl. *15*, 174 (1976).
[3] *B. Giese*, Chem. Ber. *108*, 2978 (1975).
[4] Nomenclature: *G. A. Olah*, Angew. Chem. *85*, 183 (1973); Angew. Chem. Int. Ed. Engl. *12*, 173 (1973).
[5] *B. Giese*, Chem. Ber. *108*, 2998 (1975).
[6] The small standard deviations in the differences between the entropies of activation were accomplished by multiple measurement of the experimental values over a temperature range of 120°.

X-Ray Structure Analysis of 6-Methyl-6-oxo-3,5,7-triphenyl-6λ⁵-phosphatricyclo[3.3.1.0²,⁷]non-3-ene, the Product of Unusual Intramolecular Reactions

By *Werner J. Seifert*, *Ortwin Schaffer*, and *Karl Dimroth*[*]

Dedicated to Professor H. H. Inhoffen on the occasion of his 70th birthday

While investigating the rearrangement reactions of derivatives of λ⁵-phosphorin we found that the phospha-2,4-cyclohexadiene derivative *(2)*, formed *via* a $[3_s5_s]$ and a subsequent $[3_s3_s]$ rearrangement on heating of 1-allyloxy-1-methyl-2,4,6-triphenyl-λ⁵-phosphorin *(1)*, is itself transformed in boiling



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toluene into the stable well-crystalline product of an intramolecular Diels-Alder reaction. Due to the complicated ^{1}H-NMR spectrum it could not be decided unequivocally if the five-membered or the four-membered ring derivative, *(3)* or *(4)*, had been formed[1]. Although postulated as intermediates of allyl phenyl ether rearrangements, intramolecular [4+2] cycloadducts have not yet been isolated[2]; such isolation has only been accomplished in the thermal rearrangement of propargyl phenyl ethers[3]. Thermolysis of 7-allyloxycycloheptatriene afforded a mixture of tricyclic reaction products of various ring sizes[4].

X-Ray structure analysis of the stable rearrangement product *(3)* or *(4)* has now permitted a decision in favor of the structural alternative *(4)*, and also confirmed that both rearrangement steps *(1)* → → *(2)* proceed suprafacially because the oxo group attached to phosphorus is located on the same side of the ring plane as the carbocyclic bridge newly formed from *(2)* by cycloaddition.

Compound *(4)* crystallizes in the triclinic space group $P\bar{1}$ with $a=9.940$, $b=12.164$, $c=10.660$ Å; $\alpha=82.11$, $\beta=115.25$, $\gamma=110.25°$; $Z=2$; $d_{calc.}=1.21\,g\,cm^{-3}$. A single crystal (*ca.* $0.5\times0.5\times0.2$ mm) was mounted on an automated Nonius four-circle diffractometer ($Mo_{K\alpha}$ radiation) and 2931 independent reflections registered, 2555 with detectable intensity, $Fo \geq \delta(Fo)$. The structure was solved by direct methods (MULTAN program[5]). The coordinates of all atoms (except H) could be deduced from an *E* Fourier synthesis with 350 phased reflections ($E \geq 1.60$). Refinement with anisotropic temperature factors for the P, O, and C atoms, and with isotropic temperature factors for the H atoms converged at $R=4.3\%$ (observed reflections).

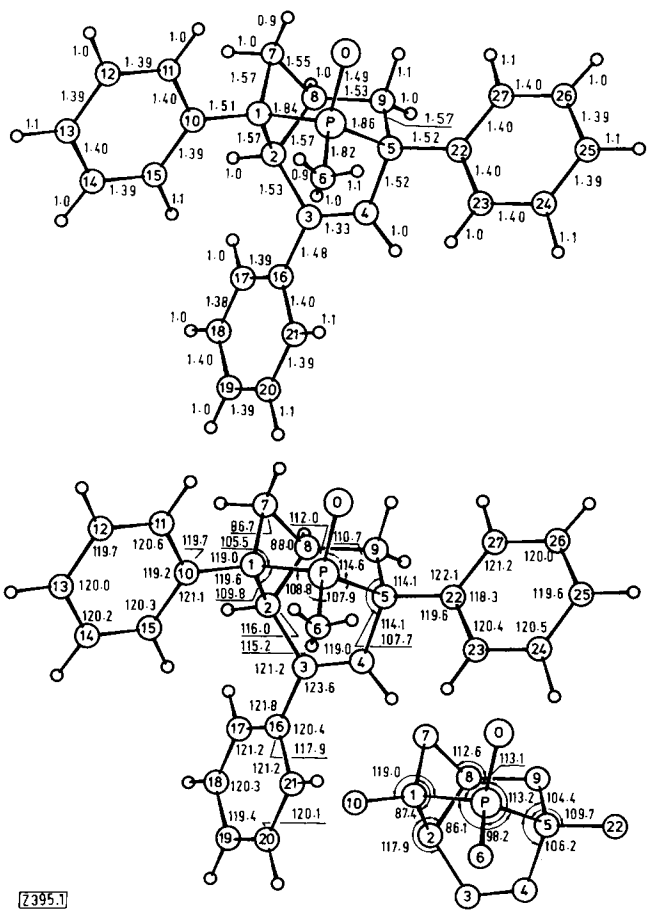

Fig. 1. Molecular structure of *(4)* with bond lengths [Å] (above) and angles [°] (below); mean standard deviations 0.004 Å (except for C—H: 0.04 Å) and 0.3°. The bond lengths are not corrected. Atoms designated by a number only are C atoms.

The tricyclic molecular skeleton of *(4)* is conformationally rigid. The bond lengths and angles (cf. Fig. 1) largely agree with the values obtained for analogous building units[6]. The bond angles in the four-membered ring are smaller than 90°; the pronounced folding (dihedral angle 35.6°) is attributable to the strained bridge between C-8 and C-5.

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CAS Registry numbers:
(1), 54191-94-5; *(2)*, 58485-95-3; *(4)*, 58525-84-1

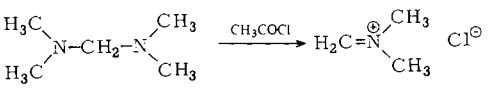
[1] *O. Schaffer* and *K. Dimroth*, Angew. Chem. *87*, 136 (1975); Angew. Chem. Int. Ed. Engl. *14*, 112 (1975).
[2] *P. Fahrni* and *H. Schmid*, Helv. Chim. Acta *42*, 1102 (1959); *H. J. Hansen* and *H. Schmid*, Chem. Br. *5*, 111 (1969).
[3] *J. Zsindely* and *H. Schmid*, Helv. Chim. Acta *51*, 1510 (1968).
[4] *Ch. A. Cupas*, *W. Schumann*, and *W. E. Heyd*, J. Am. Chem. Soc. *92*, 3237 (1970).
[5] *G. Germain*, *P. Main*, and *M. M. Woolfron*, Acta Crystallogr. *A 27*, 368 (1971).
[6] *Mazar-Ul-Roque* and *C. N. Caughlan*, Chem. Commun. *1968*, 1228; *T. N. Margulis*, Acta Crystallogr. *19*, 857 (1965).

A New Variant of the Mannich Reaction[**]

By *Günther Kinast* and *Lutz-F. Tietze*[*]

The Mannich reaction is one of the most important methods available for the α-aminoalkylation of CH acidic compounds[1]. In general, a carbonyl component—usually formaldehyde—, a secondary amine, and a CH acidic compound are allowed to react together. Serious drawbacks of these reaction conditions include long reaction times, difficult optimization, poor reproducibility of the results, and the occurrence of side reactions.

We have now shown that *N,N*-dimethyl(methylene)ammonium chloride *(2)* is an inexpensive and extremely convenient reagent for α-aminoalkylation of ketones and aldehydes.



(1) *(2)*

The salt *(2)* is prepared from the aminal *(1)* and acetyl chloride in ether[2]. It crystallizes from the reaction solution and can be used without further purification. The compound can be stored indefinitely in the absence of moisture.

In order to perform the Mannich reaction, compound *(2)* (10 mmol) is suspended in anhydrous acetonitrile (5 ml) and stirred with a 10% excess of the aldehyde or ketone *(3)* for 2 min at 82 °C or 120 min at 20 °C, if necessary with cooling. The reaction time must be increased for less reactive ketones. In the course of the reaction, the reagent *(2)* dissolves and the α-aminoalkylated aldehydes or ketones generally crystallize spontaneously in the form of the hydrochlorides *(4)*. Yields are usually very good and the crystalline products often already analytically pure (Table 1).

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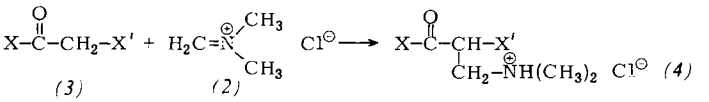
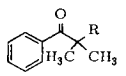
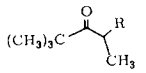
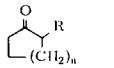
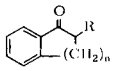
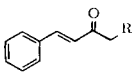
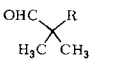
[**] This work was supported by the Deutsche Forschungsgemeinschaft.

Table 1. Aminoalkylation of aldehydes and ketones *(3)*, R = H, with *N,N*-dimethyl(methylene)ammonium chloride to form aminomethyl-aldehydes and -ketones in the form of the hydrochlorides *(4)*, R = $-CH_2-\overset{\oplus}{N}H(CH_3)_2\ Cl^{\ominus}$.



(3) *(2)* *(4)*

	(3), *(4)*	Reaction temp./time [°C]/[min]	M.p. [°C]	*(4)* Yield [%] [a]	Comparison Yield [%]	Ref.
a		82/45	128	53 (78)	6 [b]	[3]
b		82/45	144	58 (86)	—	—
c	 n = 1	82/2 20/120	148—149	79 82	60 [b]	[4]
d	n = 3	82/2 20/120	131—133	55 72 (85)	37 [b]	[5]
e	 n = 1	82/10	148—150	96	86	[6]
f	n = 2	82/10	144—145	97	65	[7]
g	n = 3	82/10	145—146	97	40	[8]
		20/120	157	84	25	[9]
i		82/2 20/120	152	79 87	—	[10]
j		82/2 20/120	151—153	81 82	—	[11]

[a] Yields of crystalline product; average values of several runs. Values in parentheses: overall yields after workup to give the amino ketone.
[b] Yields of amino ketone.

The data listed in Table 1 demonstrate the superiority of aminoalkylation with the iminium salt *(2)* over the "classical" Mannich reaction. In particular, the new method can also be employed for the reaction of sterically hindered ketones [*e.g. (3a)* and *(3b)*]. Unsymmetrical ketones [*e.g. (3i)*] are almost exclusively aminoalkylated at the more highly substituted C atom.

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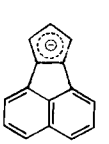
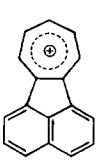
CAS Registry numbers:
(1), 51-80-9; *(2)*, 30354-18-8; *(3a)*, 611-70-1; *(3b)*, 564-04-5; *(3c)*, 120-92-3; *(3e)*, 83-33-0; *(3h)*, 122-57-6; *(3i)*, 1120-72-5; *(3j)*, 78-84-2; *(4a)*, 24206-69-7; *(4b)*, 58485-89-5; *(4c)*, 42746-87-2; *(4e)*, 16931-84-3; *(4h)*, 5409-51-8; *(4i)*, 58485-90-8; *(4j)*, 29392-33-4; CH_3COCl, 75-36-5

[1] *M. Tramontini*, Synthesis *1973*, 703, and references cited therein.
[2] Prepared in analogy to a procedure reported by *H. Böhme*, *H. Böhme*, and *K. Hartke*, Chem. Ber. *93*, 1305 (1960).
[3] *J. K. Coward* and *T. C. Bruice*, J. Am. Chem. Soc. *91*, 5339 (1969).
[4] *M. Mousseron*, *R. Jacquier*, and *H. Christol*, Bull. Soc. Chim. Fr. *1957*, 346.
[5] *W. Treibs* and *M. Mühlstaedt*, Chem. Ber. *87*, 407 (1954).
[6] *G. L. Buchanan*, *A. C. W. Curran*, *J. M. McCrae*, and *G. W. McLay*, Tetrahedron *23*, 4729 (1967).
[7] *C. Mannich*, *F. Borkowsky*, and *W. H. Lin*, Arch. Pharm. (Weinheim) *275*, 54 (1937).
[8] *J. Brugidou* and *H. Christol*, Bull. Soc. Chim. Fr. *1966*, 1693.
[9] *H. B. Nisbet*, J. Chem. Soc. *1938*, 1237.
[10] *H. O. House* and *B. M. Trost*, J. Org. Chem. *29*, 1339 (1964).
[11] *C. Mannich*, *B. Lesser*, and *F. Silten*, Ber. Dtsch. Chem. Ges. *65*, 378 (1932).

The Cyclohept[*a*]acenaphthylenylium Ion

By *Kagetoshi Yamamoto* and *Ichiro Murata*[*]

Among the many hydrocarbon cations so far studied the cyclohepta[*cd*]phenalenylium ion ($pK_{R^+} \approx 8.4$)[1] was found to be particularly stable. A recent study[2] revealed that the thermodynamic stability of the cyclopentadienyl anion is enhanced by annelation of the acenaphthylene system to give the anion *(1)*; this suggests the cyclohept[*a*]acenaphthylenylium ion *(2)* to be a highly stabilized hydrocarbon cation.

(1)   *(2)*

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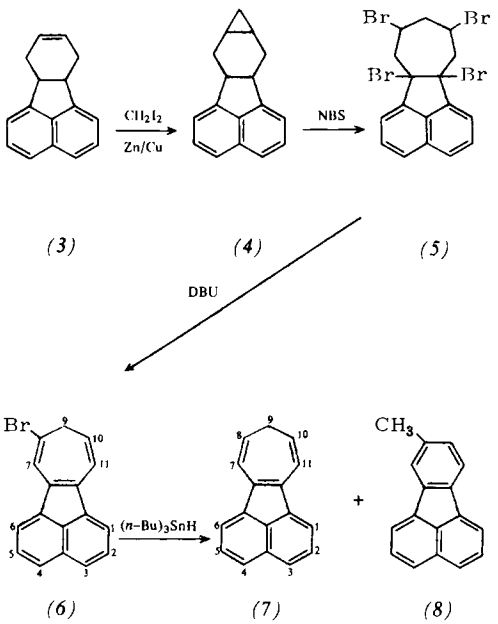
The pentaphenylcyclohept[*a*]acenaphthylenylium ion was first synthesized in 1963[3]. We have now synthesized the parent cation *(2)*, and believe it to be the most stable hydrocarbon cation yet known.



(3) *(4)* *(5)* *(6)* *(7)* *(8)*

The starting material for the synthesis was 6b,7,10,10a-tetrahydrofluoranthene *(3)*[4] which was cyclopropanated *via* the Harrison modification[5] of the Simmons-Smith reaction to produce the norcarane derivative *(4)*. Compound *(4)*, m.p. 67—68 °C, was purified by chromatography on a silver-nitrate-impregnated silica gel column with hexane (40—50 % yield). Treatment with four equivalents of NBS in benzene at room temperature afforded the crude tetrabromide *(5)* in 27 % yield, which was utilized in subsequent transformations. Dehydrobromination of *(5)* with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[6] (in THF at ambient temperature, 12 h, under N_2) followed by chromatographic separation of the products (silica gel, hexane) gave the pure monobromide *(6)*, orange plates, m. p. 105—109 °C. The structure of *(6)* is clearly supported by its ^{1}H-NMR spectrum.

Reduction of *(6)* in refluxing toluene with tri-*n*-butyltin hydride leads to 9*H*-cyclohept[*a*]acenaphthylene *(7)* in addition to a small amount of unidentified hydrocarbon presumed to be 8-methylfluoranthene *(8)* in a ratio of 7 : 3[7]. Compound *(7)* showed the following ^{1}H-NMR characteristics after subtracting the spectrum of *(8)*: $\delta = 2.61$ (t, $J_{9,8} = J_{9,10} = 7.0$ Hz, 2 H-9), 5.58 (dt, $J_{8,7} = J_{10,11} = 9.0$, $J_{8,9} = J_{10,9} = 7.0$ Hz, H-8, H-10), 6.98 (d, $J_{7,8} = J_{11,10} = 9.0$ Hz, H-7, H-11), 7.4—7.9 ppm (m, H-1 to H-6).

Since we were unable to obtain *(7)* free of *(8)* by repeated chromatography, the final synthetic step was carried out with the mixture. Hydride abstraction from *(7)* was accomplished by treating the mixture in dry chloroform with trityl tetrafluoroborate. We obtained the cation *(2)* as the tetrafluoroborate [reddish orange crystals which decomposed at 163—170 °C; UV (acetonitrile): $\lambda_{max} = 263$ nm ($\log\varepsilon = 4.31$), 333 (4.44), 438 (4.23); 100-MHz ^{1}H-NMR (CF_3COOD): $\delta = 8.28$ (t, $J = 8.1$ Hz, H-2, H-5), 8.74 (d, $J = 8.1$ Hz, H-3, H-4), 9.04 (d, $J = 8.1$ Hz, H-1, H-6), 8.9—9.1 (m, H-8 to H-10), and 9.7 ppm (m, H-7, H-11)]. The NMR spectrum was consistent with the extensive charge delocalization into the naphthalene moiety. The species *(2)* is far more stable than other annulated tropylium ions[8]; its pK_{R^+} value is 8.7 (determined by a standard spectrophotometric method in 20 % aqueous acetonitrile). These results clearly indicate the effect of the acenaphthylene unit in delocalizing the positive charge of the tropylium ion.

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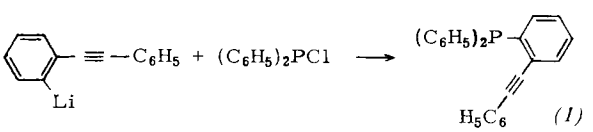
CAS Registry numbers:
(2), 58526-68-4; *(3)*, 58485-91-9; *(4)*, 58485-92-0; *(5)*, 58485-93-1; *(6)*, 58485-94-2; *(7)*, 206-85-9; *(8)*, 20485-57-8

[1] *I. Murata, K. Yamamoto,* and *Y. Kayane,* Angew. Chem. *86*, 862 (1974); Angew. Chem. Int. Ed. Engl. *13*, 808 (1974).
[2] *K. Yamamoto, M. Morioka,* and *I. Murata,* Tetrahedron Lett. *1975*, 3009.
[3] *M. A. Battiste,* J. Am. Chem. Soc. *85*, 2175 (1973).
[4] *M. C. Kloetzel* and *H. E. Mertel,* J. Am. Chem. Soc. *72*, 4786 (1950).
[5] *R. J. Rawson* and *I. Harrison,* J. Org. Chem. *35*, 2057 (1970).
[6] We thank San-Abbott Ltd. for gift of DBU.
[7] Determined by NMR integration. *(8)* shows characteristic ^{1}H-NMR methyl absorption at $\delta = 2.46$ ppm.
[8] *E. Heilbronner* and *H. Bock:* Das HMO-Modell und seine Anwendung. Verlag Chemie, Weinheim 1968, Vol. 1, p. 355.

2,2″-Bis(diphenylphosphino)-2′,3′,5′,6′-tetraphenyl-*p*-terphenyl as an Arene Chelate Ligand for Rhodium(I)

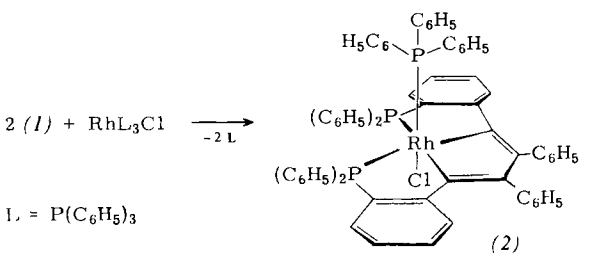
By *Werner Winter*[*]

Monoalkynylphosphanes react with transition metal compounds to give, *e.g.*, polynuclear complexes containing not only coordinated P atoms but also oligomerized "acetylene structures"[1]. Steric constraints preclude formation of a mononuclear chelate complex by the $R_2P{-}C{\equiv}C{-}R'$ group. However, this should be possible in the case of the vinylogous *o*-phenylethynyltriphenylphosphane *(1)*, preparable from *o*-lithiotolan and diphenylchlorophosphane as colorless crystals having melting point 93—94 °C (cyclohexane) [IR (KBr): $\nu(C{\equiv}C) = 2210\,cm^{-1}$ (w); FT-^{31}P{^{1}H}-NMR ($CHCl_3$, H_3PO_4 as external reference): $\delta = +8.4$ ppm; MS: $m/e = 362$ (M^+); yield 86 %].



(1)

Stirring of *(1)* and $RhCl(PPh_3)_3$ (molar ratio 2 : 1) in CH_2Cl_2 at room temperature for several minutes affords the octahedral rhodacyclopentadiene chelate complex *(2)* [obtained as orange-yellow needles, m.p. 230 °C, on slow precipitation with *n*-hexane, yield 80 %].



(2)

The composition and structure of the diamagnetic Rh^{III} complex follow from elemental analysis, osmometric molecular weight determination, conductivity measurements (nonelectrolyte!), and above all from the FT-^{31}P{^{1}H}-NMR spectrum

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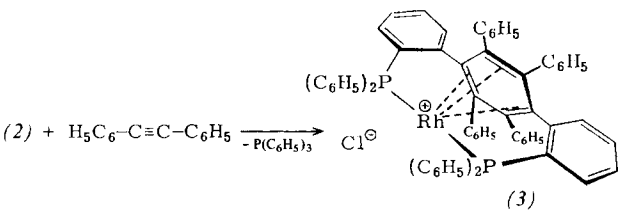
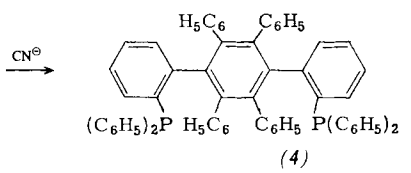
(CH_2Cl_2, H_3PO_4 as external reference): owing to anisotropic effects of the phenyl groups in a propeller-type arrangement on the apical triphenylphosphane ligands the equatorial chelate P atoms are found to give separate quadruplets at $\delta = -34.9$ and -28.6 ppm [$J_{RhP} = 115$, $^2J_{P(a)-P} = 29$, $^2J_{P-P} < 5$ Hz], whereas the apical P atom produces two triplets at $\delta = -8.7$ ppm [$J_{RhP(a)} = 94$, $^2J_{P(a)-P} = 29$ Hz]; in particular, the J_{RhP} values are typical for Rh^{III} complexes[2, 3].

The structure of *(2)* is also confirmed by the the IR spectrum (absence of ν(C≡C) vibrations) and by the reaction with tolan in boiling xylene: the ionic η^6-arene chelate Rh^I complex *(3)*, which is insoluble in xylene, appears almost instantaneously.





The orange-yellow, likewise diamagnetic "[4+2] cycloadduct" *(3)* [m.p. 370 °C; yield 87 %] can also be characterized by elemental analysis, molecular weight determination, conductivity measurement ($\Lambda_M = 71.4\ cm^2\ \Omega^{-1}\ mol^{-1}$, nitromethane, 1:1 electrolyte[4]) and the ^{31}P-NMR spectrum: $\delta = -48.9$ ppm, d, $J_{RhP} = 203$ Hz (typical for Rh^I complexes). The FT-$^{13}C\{^1H\}$-NMR spectrum contains the upfield shift of the new arene ligand at $\delta = 105$ ppm (narrow multiplet, coupling with ^{31}P and ^{103}Rh).

Heating of *(3)* with NaCN in aqueous ethanol affords the free ligand 2,2″-bis(diphenylphosphino)-2′,3′,5′,6′-tetraphenyl-*p*-terphenyl *(4)* [colorless crystals, m.p. 320—322 °C (benzene); ^{31}P-NMR ($CHCl_3$, H_3PO_4 as external reference): $\delta = +13.3$ ppm; MS: $m/e = 902$; yield 82 %].

The complexes *(2)* and *(3)* are extremely stable thermally and can be kept indefinitely in air. The possibility of *(3)* existing as a coordinatively unsaturated 16-electron system in the η^4-arene form is unlikely because this compound is completely inert towards CO in CH_2Cl_2[5].

The chelate function of the tertiary bisphosphane in *(2)* and *(3)* accounts for this, the first isolation of the Rh-arene intermediate[6] long suspected to occur in the Rh-catalyzed trimerization of acetylene. The reaction sequence *(1)* → *(4)* opens up a new entry to the hitherto unknown (*p*-terphenyl-2,2″-ylene)bisphosphanes, which hold promise as essentially rigid chelate ligands of fixed geometry.

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CAS Registry numbers:
(1), 58581-32-1; *(2)*, 58602-35-0; *(3)*, 58602-36-1; *(4)*, 58581-32-2; *o*-lithiotolan, 42168-23-0; $(C_6H_5)_2PCl$, 1079-66-9; $Rh(P(C_6H_5)_3)_3Cl$, 14694-95-2; tolan, 501-65-5

[1] *N. K. Hota, H. A. Patel, A. J. Carty, M. Mathew*, and *G. J. Palenik*, J. Organometal. Chem. *32*, C 55 (1971); *T. O'Connor, A. J. Carty, M. Mathew*, and *G. J. Palenik, ibid. 38*, C 15 (1972); *N. J. Taylor, H. N. Paik, P. C. Chieh*, and *A. J. Carty, ibid. 87*, C 31 (1975).

[2] Cf. *W. Winter*, Angew. Chem. *87*, 172 (1975); Angew. Chem. Int. Ed.
[3] *W. Winter*, J. Organometal. Chem. *92*, 97 (1975).
[4] *W. J. Geary*, Coord. Chem. Rev. *7*, 81 (1971).
[5] Cf. *R. R. Schrock* and *J. A. Osborn*, Inorg. Chem. *9*, 2339 (1970).
[6] *R. Burt, M. Cooke*, and *M. Green*, J. Chem. Soc. *A 1970*, 2981.

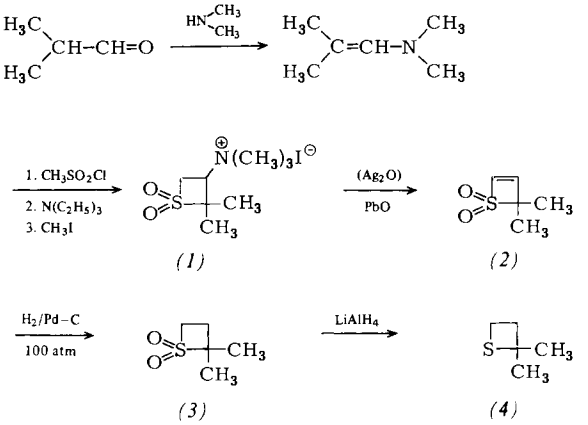
Mustelan, the Malodorous Substance from the Anal Gland of the Mink *(Mustela vison)* and the Polecat *(Mustela putorius)*[**]

By *Hermann Schildknecht, Ingrid Wilz, Franz Enzmann, Norbert Grund*, and *Manfred Ziegler*[*]

We have taken advantage of the ready availability of mink posteriors to isolate from their anal glands the typical malodorous substance of species of the marten family (Mustelidae)[1]. Preparative gas chromatography of the yellow to green paste obtained from the secretion reservoir of similar size to a hazel nut in the anal sac yielded the penetratingly odorous compound mustelan as major component [255 mg from 450 anal sacs; 30 % loaded Apiezon L column (10″ × 3/8″); temperature program 136 to 236 °C].

Mustelan, b.p. 115 °C, is a mobile and colorless liquid, which according to elemental analysis and mass spectrometry has the molecular formula $C_5H_{10}S$. Absorption spectral studies and, in particular, the fragments obtained on electron pyrolysis[2], *viz.* 1-isopentanethiol, isopropyl alcohol, ethanol, and ethylene, suggested 2,2-dimethylthietane *(4)* to be the malodorous substance of the mink. This result was confirmed by desulfuration with Raney nickel to give isopentane. We found the 60-MHz ^{1}H-NMR spectrum ($CDCl_3$, TMS = 0) of mustelan to contain a singlet at 1.53 (6H) and two multiplets of an AA′BB′ system at *ca.* 2.68 and *ca.* 3.0 ppm (2H each); they are due to the ring methylene groups. Final proof of structure was provided by synthesis[3].

The best synthetic strategy appeared to involve the thietane 1,1-dioxide *(3)* which can easily be reduced to the thietane *(4)*. However, sufficient amounts of pure *(4)* for further tests only became available once we had succeeded in degrading the salt *(1)* with the less expensive PbO instead of Ag_2O. X-Ray structure determination of *(3)* expectedly showed that the thietane ring is nonplanar[4]. The new synthesis developed by *Mayer*[5] is particularly suitable for preparing larger quantities of mustelan.



[*] Prof. Dr. H. Schildknecht, Dr. I. Wilz, Dr. F. Enzmann, Dr. N. Grund, and Prof. Dr. M. Ziegler
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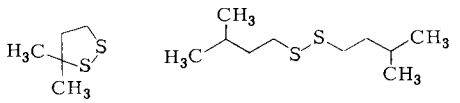
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Workup of the anal secretion of the mink by gas chromatography also gave 20 mg of a dark yellow, readily polymerizing oil whose IR spectrum closely resembles that of *(4)*, except for an additional band at 993 cm^{-1}. This fraction was shown to be 3,3-dimethyl-1,2-dithiolane *(5)*, mainly by mass spectrometric analysis, and in particular by the base peak at $m/e=69$ (M^+-65). The isomeric 4,4-dimethyl derivative could be ruled out by comparing the UV spectrum of *(5)* with those of five other dithiolanes.



(5)

(6)

In addition to *(4)* and *(5)* we also isolated a compound (retention time 14 min at 243 °C) having a mercaptane type odor, which we deduced to be diisopentyl disulfide *(6)* from its mass spectrum. Finally, we isolated a hydrocarbon $C_{10}H_{20}$, which was not further characterized, and indole.

The malodorous substances of the weasel (*M. erminea* L.) and of the polecat (*M. putorius* L.) were compared with those of the mink by gas chromatography. Indole and the hydrocarbon $C_{10}H_{20}$ were found in the weasel, and also *(4)*, *(5)*, and *(6)* in the polecat.

Received: January 14, 1976 [Z 385 IE]
German version: Angew. Chem. *88*, 228 (1976)

CAS Registry numbers:
(3), 31462-45-0; *(4)*, 55022-72-5; *(5)*, 58384-57-9; *(6)*, 2051-04-9; *(7)*, 58375-01-2

[1] *I. Wilz*, Dissertation, Universität Heidelberg 1967.
[2] *H. Schildknecht* in *F. Korte*: Methodicum Chimicum. Vol. 1, Part 1. Thieme, Stuttgart 1973, p. 524.
[3] *N. Grund*, Dissertation, Universität Heidelberg 1972.
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Enantioselective Wagner-Meerwein Rearrangement in Chiral Solvents under High Pressure[**]

By *Hans Plieninger* and *H. P. Kraemer*[*]

Dedicated to Professor Karl Freudenberg on the occasion of his 90th birthday

Only a few enantioselective reactions are known to take place in a chiral medium without the latter entering into reaction[1]. The object of our study was to establish whether enantioselective syntheses can be induced in a chiral medium by employing high pressures.

We based our investigations on the known fact that reactions in which at least partial charges occur in the transition state have a strongly negative activation volume under high pressure (*ca.* 10^4 bar)[2]. This "electrostriction" is due to increased interaction of the solvent molecules with the partially charged atoms of the molecules participating in the transition state. Use of a chiral solvent and a starting molecule having a prochiral functional group should give rise to two diastereomeric transition states under high pressure whose different energy content must be due only to interaction with the solvent and thus be a function of the pressure.

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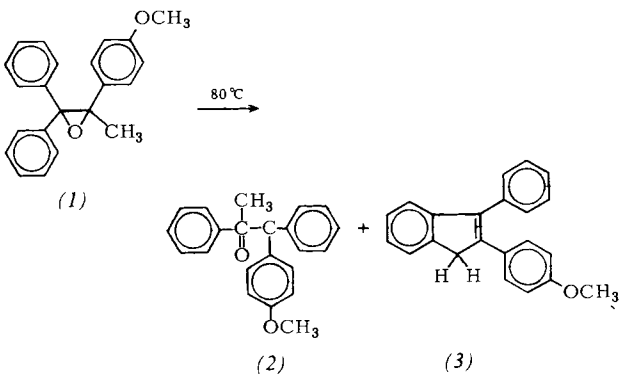
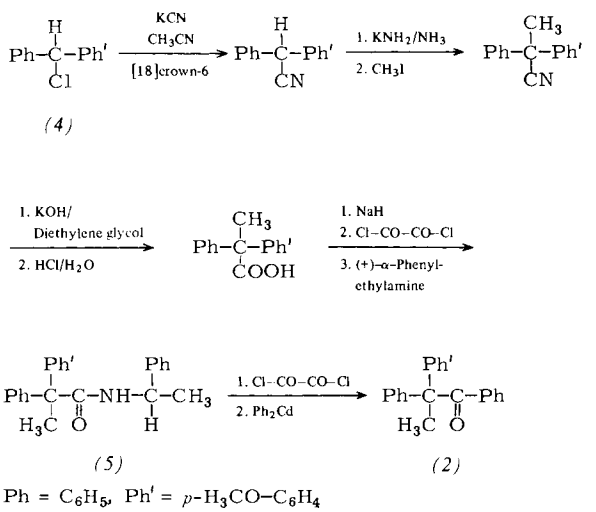
[**] This work was supported by the Deutsche Forschungsgemeinschaft.

We have investigated the rearrangement of racemic 1-(4-methoxyphenyl)-1-methyl-2,2-diphenyloxirane *(1)* in L-(+)-diethyl tartrate at atmospheric pressure and at 10^4 bar. After hydrolysis of the L-(+)-tartrate, the main product 2-(4-methoxyphenyl)-2-phenylpropiophenone *(2)* could be easily separated chromatographically from any 2-(4-methoxyphenyl)-3-phenylindene *(3)* formed as by-product. The structures of *(2)* and *(3)* were confirmed by elemental analyses and ^{1}H-NMR and IR spectra. The ratio of *(2)* to *(3)* is shifted strongly in favor of *(3)* by pressure. Compound *(2)* (57 %) obtained under high pressure (10^4 bar) proved to be optically active; $[\alpha]_{436}^{25}=-1.1°$ ($c=3.5$; $CHCl_3$). The same reaction carried out at atmospheric pressure, however, affords optically inactive *(2)* (85 %). In order to confirm that the optical activity was not due to the optically active solvent, the compound *(2)* obtained at high pressure was recrystallized several times from different solvents (2 × ethanol, 2 × ligroin).



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

To determine the degree of asymmetric induction we prepared both enantiomers of *(2)* in optically pure form from racemic 4-(α-chlorobenzyl)anisole *(4)* [*(2)* could not be resolved]. Compound *(5)* (see Scheme) was separated by column chromatography into the diastereomers *(5a)* and *(5b)*, which on treatment with oxalyl chloride and diphenylcadmium furnished the enantiomers *(2a)* $[[\alpha]_{436}^{25}=+16.24$ ($c=1.52$, $CHCl_3$)] and *(2b)* $[[\alpha]_{436}^{25}=-16.10$ ($c=0.43$, $CHCl_3$)], respectively.



(4)

(5) *(2)*

Ph = C_6H_5, Ph' = p-H_3CO-C_6H_4

The asymmetric induction found in L-(+)-tartrate at high pressure corresponds to an optical yield of $p=6.7$ %. Highly optically active *(2)* is likewise formed in other chiral solvents, *e.g.* menthol or fenchone, but its purity still has to be checked.

To our knowledge this constitutes the first enantioselective synthesis effected by pressure in a chiral medium.

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CAS Registry numbers:
(1), 58375-19-9; (±)-(2), 58375-47-0; (2a), 58375-48-1; (2b), 58375-49-2; (3). 58375-20-5: (4). 58375-21-6: (5a). 58375-22-7: (5b). 58375-23-8: oxalyl chloride. 79-37-8: diphenylcadmium. 2674-04-6

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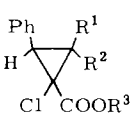
1-Cyclopropene-1-carboxylates from 1-Chloro-1-cyclopropanecarboxylic Acids[**]

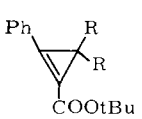
By *Volker Sander* and *Peter Weyerstahl*[*]

The isolation of a 1-cyclopropene-1-carboxylic acid has so far been accomplished in only one special case by lithiation and carboxylation of 1,3,3-trimethyl-1-cyclopropene[1]. Attempts to obtain such acids by basic HBr-elimination[2] or thermal cleavage of acetic acid[3] from cyclopropanecarboxylic acids have failed.

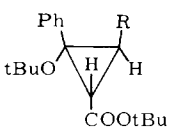
We have now synthesized the 1-cyclopropene-1-carboxylates *(5)* and *(6)* by removal of HCl from the 1-chloro-1-cyclopropanecarboxylates *(3b)* and *(4b)* with potassium *tert*-butoxide in THF. Few by-products are formed. We have already prepared other cyclopropene derivatives in this way[4]. The esters *(1b)*—*(4b)* were obtained from the carboxylic acids *(1a)*—*(4a)* by reaction with isobutylene. The acids themselves are readily accessible from the 1,1-dichlorocyclopropanes by halogen-metal exchange and carboxylation (Table 1).



(1) - *(4)*
(a), R^3 = H
(b), R^3 = tBu



(5), R = CH_3
(6), R = Ph



(7), R = H
(8), R = CH_3

Table 1. Synthesized acids *(1a)*—*(4a)*, R^3 = H, and esters *(1b)*—*(4b)*, R^3 = tBu. The ^{1}H-NMR and mass spectra are consistent with the given structures.

	R^1	R^2	*(a)* M.p. [°C]	*(b)* M.p. [°C] B.p. [°C/torr]
(1)	H	H	96	46
(2)	H	CH_3	147	60/0.05
(3)	CH_3	CH_3	151	80/0.02
(4)	Ph	Ph	190	141

As expected the 1-cyclopropene-1-carboxylic esters *(5)* and *(6)* (Table 2) are unusually strong Michael acceptors which can be isolated only if both sides of the ring bear bulky substituents.

Table 2. Physical properties of compounds *(5)*—*(8)*. All NMR spectra were recorded in CCl_4 [a].

(5): Oil; ^{1}H-NMR: δ = 1.41 (s, 6H), 1.55 (s, 9H), 7.5 (mc, 5H); IR: 1815, 1695 cm^{-1}; UV: 291 nm (heptane); MS: no M^+, $M^+ - C_4H_8$ 188 (44 %), $M^+ - C_4H_9$ 187 (84 %). $M^+ - CO_2C_4H_9$ 143 (100 %); high resolution: $M^+ - C_4H_9$ 187.0743, calc. 187.0749

(6): M.p. 110 °C. ^{1}H-NMR: δ = 1.59 (s. 9 H). 7.5 (mc. 15 H): IR: 1820. 1690 cm^{-1}: UV: 289 nm (heptane): MS (high resolution): M^+ 368.1773 (7 %). calc. 368.1775; $M^+ - C_4H_8$ 312.1105 (23 %), $M^+ - CO_2C_4H_9$ 267.1148 (100 %)

(7): Colorless oil; ^{1}H-NMR: δ = 1.03 (s, 9H), 1.07 (s, 9H), 1.4 (mc, 1H), 1.9 (mc, 2H), 7.2 (mc, 5H); IR: 1730 cm^{-1}; MS: no M^+, $M^+ - C_4H_8$ 234 (8 %), $M^+ - 2C_4H_8$ 178 (100 %)

(8): Colorless oil; ^{1}H-NMR: δ = 0.68 (d, J = 6.5 Hz, 3H), 0.97 (s, 9H), 1.49 (s, 9H), 1.90, 2.00 (AB system, B part as q, J = 7 + 6.5 Hz, 2H), 7.35 (mc, 5H); IR: 1730 cm^{-1}; MS: no M^+, $M^+ - 2C_4H_8$ 192 (59 %), 105 (70 %), 87 (100 %)

[a] *(8)* in $CDCl_3$ (WH-270).

In elimination experiments with potassium *tert*-butoxide *(1b)* and *(2b)* gave, in addition to polymers, only the adducts *(7)* and *(8)*, respectively, in 25—30 % yield. Even with the sterically more demanding potassium 3-ethyl-3-pentanolate *(1)* afforded small amounts of *(7)* along with large amounts of polymer. The configuration of *(8)* follows from attack by the butoxide ion from the unhindered side and from the coupling constants for *trans* cyclopropane protons.

tert-Butyl 2,3,3-triphenyl-1-cyclopropene-1-carboxylate (6)

1,1-Dichloro-2,2,3-triphenylcyclopropane (10 mmol) in a mixture of THF, ether, and petroleum ether (4:1:1 v/v; 50 ml) is treated dropwise under pure N_2 at −105 °C with butyllithium (10 mmol) in hexane, and then with an excess of pulverized CO_2. After usual workup, the valeric acid that is always present is distilled off at 50 °C/0.01 torr and the residue crystallized from ether/petroleum ether; yield 55 % *(4a)*.—A solution of *(4a)* (10 mmol) in dry ether (10 ml) is heated at 50 °C for 16 h under N_2 in a bomb-tube with *ca.* 10 g isobutylene and 0.2 g conc. H_2SO_4. After usual workup the crude *(4b)* is chromatographed on silica gel with pet. ether/ether (9:1); yield 62 %.—A solution of potassium *tert*-butoxide (2 mmol) in THF (5 ml) is added dropwise to an ice-cooled solution of *(4b)* (2 mmol) in THF (5 ml) (reagents purified according to Ref. [4]) under purified N_2. The mixture is stirred for 30 min at 0 °C and then for a further 30 min at room temperature. After addition of 50 ml CCl_4 the mixture is washed twice with NH_4Cl solution, three times with ice-water, dried over $MgSO_4$ and finally concentrated by evaporation. The crude ester *(6)* is recrystallized once from CCl_4; yield 71 %.

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CAS Registry numbers:
(1a), 58486-07-0; *(1b)*, 58486-08-1; *(2a)*, 58486-09-2; *(2b)*, 58486-10-5; *(3a)*, 58486-11-6; *(3b)*, 58486-12-7; *(4a)*, 58486-13-8; *(4b)*, 58486-14-9; *(5)*. 58486-15-0: *(6)*. 58486-16-1: *(7)*. 58486-17-2: *(8)*. 58486-18-3: 1,1-dichloro-2,2,3-triphenylcyclopropane, 33027-37-1

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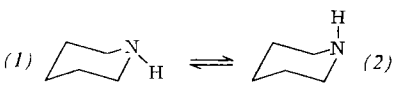
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] *G. L. Closs* and *L. E. Closs,* J. Am. Chem. Soc. *83,* 1003 (1961); *85,* 99 (1963); *I. B. Avezov, I. G. Bolezov,* and *R. Ya. Levina,* Zh. Org. Khim. (Engl. translation) *1975,* 2129.
[2] *K. B. Wiberg, R. K. Barnes,* and *J. Albin,* J. Am. Chem. Soc. *79,* 4994 (1957).
[3] *K. B. Wiberg* and *R. K. Barnes,* J. Org. Chem. *23,* 299 (1958).
[4] *K.-O. Henseling* and *P. Weyerstahl,* Chem. Ber. *108,* 2803 (1975).

Reviews

Abstracts of selected progress reports and review articles

The conformation of piperidine is discussed in an article by *I. D. Blackburne, A. R. Katritzky,* and *Y. Takeuchi.* Whether the equatorial form *(1)* or the axial form *(2)* is preferred



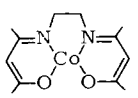
in the conformational equilibrium of piperidine has been the subject of considerable controversy (boat forms can be disregarded). In the analogous compounds with P, S^+, Se^+ or Te^+ instead of N the axial form is preferred. According to recent work it can be concluded that, for the gas phase and non-polar solvents, the piperidine equilibrium is displaced in favor of NH equatorial: $\Delta G^0 = 0.4 \pm 0.2$ kcal/mol. In hydrogen-bonding solvents, *e.g.* methanol, the position is less clear.—Piperidine derivatives with additional ring heteroatoms are also discussed. [Conformation of Piperidine and of Derivatives with Additional Ring Heteroatoms. Acc. Chem. Res. *8*, 300–306 (1975); 71 references]

[Rd 826 IE—L]

Synthetic oxygen carriers of biological interest are examined by *F. Basolo, B. M. Hoffman,* and *J. A. Ibers.* Oxygen carriers are systems forming 1:1 complexes with the O_2 molecule and in which neither the metal (M) nor the ligand (L) is oxidized irreversibly:

$$ML_n + O_2 \rightleftharpoons ML_nO_2$$

The starting point of the experiments were complexes between cobalt(II) and Schiff bases, *e.g. (1)*, which take up oxygen in the ratio 1:1. Studies on O_2—Co(porphyrin) complexes and the isolation of hemoglobin with Co in place of Fe fol-

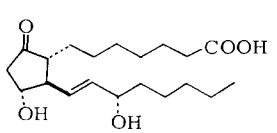


(1)

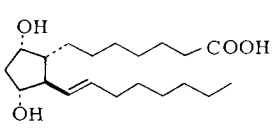
lowed. With the aid of these complexes it is possible to examine, *e.g.* the role of globin in oxygen transport. [Synthetic Oxygen Carriers of Biological Interest. Acc. Chem. Res. *8*, 384—392 (1975); 75 references]

[Rd 835 IE—L]

Prostaglandins are referred to as "Tomorrow's Drugs" in an article authored by *E. W. Horton.* The compounds prostaglandin E_1 *(1)* and $F_{1\alpha}$ *(2)* first isolated from sheep glands can be converted into many similar materials, most of which have



(1)

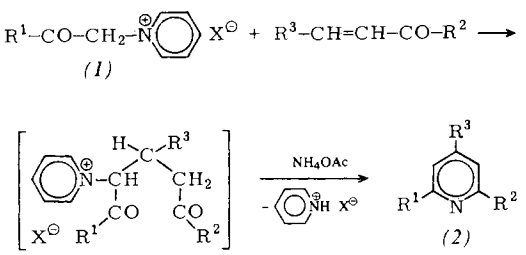


(2)

meanwhile also been found to exist in nature. They act on smooth muscle and have been used, *inter alia,* for the induction of birth, inhibition of gastric secretion, and for the relaxation of respiratory muscle. Postaglandin synthesis is blocked by aspirin and pharmacologically related substances. This effect appears to account for the action of aspirin, indomethacin, butazolidine, *etc.* Great efforts are presently being made to synthesize prostaglandins having selective activities. [Prostaglandins—Tomorrow's Drugs. Chem. Soc. Rev. *4*, 589–600 (1975); 44 references]

[Rd 839 IE—F]

The specific synthesis of substituted pyridines *(2)* **and oligopyridines** from (acylalkyl)pyridinium salts *(1)* and α,β-unsaturated ketones with ammonium acetate/glacial acetic acid or methanol is considered by *F. Kröhnke.* Individual representatives of this class of compounds are of interest for analytical applications. Bipyridine derivatives are of significance as herbicides (diquat, paraquat; some dialkylated bipyridines exhibit hypotensive, ganglion-blocking, or curare-type activity. The high reactivity of the *N*-methylene H atoms of many pyridinium salts, in particular those of type *(1)*, permit reaction with



(1) *(2)*

unsaturated ketones, or Mannich bases derived therefrom, in good yields. In place of *(1)*, 1,3-diketones and analogous compounds can be treated with α,β-unsaturated ketones; use of ammonium acetate/methanol permits ring closure to the 1,4-dihydropyridine derivative which can easily be dehydrogenated to the pyridine derivative. After a discussion of the nomenclature of the oligopyridines, the author considers the synthesis of bi-, ter-, quater-, quinque-, and septipyridines and annelated pyridines. [The Specific Synthesis of Substituted Pyridines and Oligopyridines. Synthesis *1976*, 1—24; 93 references]

[Rd 840 IE—M]

The search for life in the solar system is the title of a review by *N. H. Horowitz.* A prerequisite for life as we understand the term is the presence of complicated carbon compounds. In order to support life a planet should not be so hot as to decompose amino acids; moreover, it should also possess an atmosphere to ensure the circulation of material, including volatile metabolites. Thus living organisms could only exist on Mars and, even less likely, on Titan, the largest moon of Saturn. The Martian atmosphere is poor in water, and thus hostile to life. Much information is expected from the Martian probes Viking A and B launched in late 1975. They carry, *inter alia,* automated laboratories designed to perform biological experiments on the surface of the planet. [The Search for Life in the Solar System. Acc. Chem. Res. *9*, 1—7 (1976); 57 references]

[Rd 841 IE—L]

Several annual surveys are to be found in a volume of the Journal of Organometallic Chemistry. *C. Blomberg* has compiled the literature appearing on magnesium in 1974 (114 pp., 384 references); *G. O. Doak* and *L. D. Freedman* have authored three separate reviews of the 1974 literature on arsenic, antimony, and bismuth (102 pp., 326 references; 38 pp., 116 references; and 4 pp., 26 references). Articles on ferrocene published in the same year have been collected by *G. Marr* and *B. W. Rockett* (78 pp., 209 references). There follows a survey of the 1973 literature on nickel, palladium, and platinum by *E. Singleton*, *G. Cooke*, and *J. R. Moss* (124 pp., 463 references). The volume closes with an author index. [J. Organomet. Chem. *106*, 1—486 (1976)]

[Rd 842 IE—L]

Raw materials, as the basis of industry and primarily the chemical industry, provide the subject matter for an entire issue of the journal "Science". More than 30 authors express their ideas about future supplies of all kinds of raw materials and about possibilities of avoiding threatening shortages.—A brief introduction is followed by five articles on economic aspects and three about questions of energy and the environment and about the recovery of materials (and generation of energy) from household garbage. In the next four articles future requirements are estimated and suggestions made for action upon eventual exhaustion of, *e.g.*, mercury reserves. Production of chemicals from coal is another topic considered. There follow three contributions on prospecting for ores and new processes for extraction and recovery of metals, and three about materials for special purposes, *e.g.* in electronics. The final six articles are about wood and plant materials. These sources are the only ones capable of regeneration and therefore occupy a special position. [Materials. Science *191*, 631—776 (1976)]

[Rd 843 IE—L]

Rydberg states are considered in a review by *R. S. Mulliken*. A complete understanding of electronic spectra and the photochemistry of atoms and molecules requires a knowledge of the spectra of Rydberg states. Rydberg states are transversed during the ionization process and are also of importance for reactions in the upper atmosphere. In the case of atoms and molecules having high ionization energies the Rydberg spectra lie in the vacuum UV; for species with lower ionization energies they extend into the near UV. Particular attention is paid to H_2^+ as a prototype of a molecule and to Rydberg states in diatomic molecules such as N_2 and NO. [Rydberg States and Rydbergization. Acc. Chem. Res. *9*, 7—12 (1976); 13 references]

[Rd 844 IE—L]

BOOK REVIEWS

Technische Chemie—Eine Einführung in die chemische Reaktionstechnik (Industrial Chemistry: Introduction to the Technology of Chemical Reactions). By *E. Fitzer* and *W. Fritz*. Springer Verlag, Berlin–Heidelberg–New York 1975. 1st Edit., xiii, 532 pp., 150 figures, 36 tables, paper, DM 44.—.

This book fills a gap that has been felt for many years in the German-language literature by chemistry students and teachers in universities.

The volume is divided into two parts. In the first 3 chapters (104 pp.), the economic factors affecting production are explained and the position of the chemical industry within the framework of world production is presented. The individual parameters affecting profits, such as the production output, the range of capacity, the site of the factory, *etc.* are discussed and the criteria for the choice of the raw materials and processes are described with the aid of examples. After the concepts important for reaction techniques have been explained, the industrial realization of batch, semibatch, and flow processes is related to the properties of reactor types important for single-phase and multiphase systems, as well as to the individual aspects of process optimization and the minimization of costs.

The second part (418 pp.) forms the bulk of the book, providing quantitative relationships for a mathematical treatment of the course of the reaction. The principles of chemical thermodynamics, microkinetics and heat and material transport are treated in Chapters 4 and 5. The behavior and the properties of ideal reactor types for batch and continuous operation in isothermal, adiabatic, and polytropic processes are presented in Chapters 6 to 10. Comparison of the residence-time distributions and back-mixing for ideal and real reactors and for the diffusion and the cell model, as well as calculations of the yield for real reactors are carried out in Chapter 11. Chapters 12 to 15 treat chemical reactions in multiphase systems, the special features of heat and material transport processes in reactions at the solid-liquid interface, and the principles of catalytic and non-catalytic heterogeneous reactions, including the relevant reactors; the various possible methods of carrying out such reactions are discussed. Chapter 16 (by *H. Gerrens*) is devoted to polymerization reactions and their industrial performance.

The book is written with didactic expertise, in readily understood, clear form, and with many illustrations and numerous examples of calculations taken from practice, together with their solutions; it can be recommended as a textbook, and that not only for chemistry students, since its readership should also include many chemists and economists.

Milos Ralek [NB 297 IE]

Environmental Chemistry. Vol. 1. Specialist Periodical Reports. Senior Reporter *G. Eglinton*. The Chemical Society, London 1975. 1st Edit., xii, 199 pp., numerous figs. and tables, bound, £ 7.—.

This is the first volume of a new series of "Specialist Periodical Reports" with the subtitle "Review of Recent Literature on the Organic Chemistry of the Environment up to the Middle of 1973"; the next volume, which should treat also inorganic problems, is expected by late 1976. The intended readership goes far beyond chemists. In the first chapter the biogeochemical cycles in undisturbed and stressed environmental regions are treated by the use of the stable isotopes of C, S, N, H, and O as examples; three chapters deal with ecotypes determined by water, with inclusion, when necessary, of sedimentary chemistry, material balances, and the microbiology of these areas. Two further chapters describe hydrocarbons in marine systems, including oil-spill accidents, as well as the behavior of DDT and PCB, with emphasis on metabolism, distribution, and analysis. In the final chapter 2,4-dichlorophenoxyacetate is discussed in detail. The text of the seven chapters is excellently documented with formulas, tables, and more than 900 references; the large number of diverse literature sources alone shows how much work of compilation has gone into this volume, which is a real mine of information for the user. The volume fulfills the function of a mediator

between the specialists and the large circle of other scientists who are, or may be compelled to be, interested in environmental problems.

Günther Siebert [NB 300 IE]

Elektrolytgleichgewichte und Elektrochemie (Electrolytic Equilibria and Electrochemistry). Fachstudium Chemie, Lehrbuch 5. By *G. Ackermann, W. Jugelt, H.-H. Möbius, H. D. Suschke*, and *G. Werner*. Verlag Chemie, GmbH, Weinheim 1975. 1st Edit., 292 pp., 83 figs., 66 tables, paperback, DM 34.—.

This book contains ten chapters: solutions, electrolyte theory, electrochemical equilibria, electrochemical processes, acid-base equilibria, redox equilibria, precipitation equilibria, complex equilibria, extraction equilibria, and ion-exchange equilibria. The classical thermodynamics of ions in solution are treated in detail, the student being offered a good introduction; this is the strength of the book. The attached chapter "Electrochemistry" is, however, very short, with thermodynamics in predominance; thus, there is no discussion of modern electroanalytical methods or of industrial applications of electrochemistry. The Debye-Hückel theory is introduced in the form of its results only but is not derived.

Sections in small print provide the reader with additional information, some of it on still controversial topics. It is in particular here that the absence of literature references proves a great disadvantage. The indicative treatment of these fields—nonaqueous solvents and acid-base theories, for example—provides too little for the student.

The classifications of cations according to *Schwarzenbach, Ahrland, Chatt* and *Davies*, and *Pearson*'s concept of hard and soft acids and bases are not kept separate. In Table 8.2 Ga^{3+} is classified as soft but on p. 142 as hard.

The thermodynamic principles of extraction, of precipitation equilibria and ion-exchange equilibria are well treated, analytical and industrial processes being also indicated. To prevent mere reading without understanding, questions are built into the text and further problems are given at the end of each chapter, which is a help for independent study.

Gerhard Gritzner [NB 303 IE]

Auswertung und Analyse kinetischer Messungen (taschentext 37) (Evaluation and Analysis of Kinetic Measurements (pocketbook 37)). By *E. S. Swinbourne*. Revised and translated by *O. F. Olaj*. Verlag Chemie/Physik Verlag, Weinheim 1975. x, 166 pp., 36 figures, 47 tables, bound, DM 17.80.

The two middle chapters "Regularity and Order of Chemical Reading" (Chapter 3) and "Determination of the Rate Constants" (Chapter 4) of the book are concerned with the evaluation and analysis of kinetic measurements. In two general chapters the reader is familiarized with the numerical and graphical methods of data analysis and the most important prerequisites of error theory. The final chapter 5 provides stimulation and indicates special problems.

The book does not require any mathematical background beyond that taught in a Grammar School and that could not be mastered with the aid of the book itself. The many examples worked out for the reader are useful. The clear and simple structure of the book leads the beginner directly to the field of application, analysis of kinetic data with the aid of simple methods.

Josef Barthel [NB 304 IE]

Russian-English Chemical and Polytechnical Dictionary. By *Ludmilla I. Callaham*. John Wiley & Sons, New York—London 1975. 3rd Edit., xxviii, 852 pp., bound, £ 18.95.

This dictionary is the result of more than thirty years of involvement with Russian technical literature. In 852 pages printed in two columns it contains a wealth of carefully selected Russian terms (the number of entries is estimated at 80000—90000) from inorganic, organic, physical, analytical, and nuclear chemistry as well as from industrial chemistry (from the plastics, fiber, ceramic, paper, foodstuffs, dyes and varnishes, fertilizer, pest control, and pharmaceutical industries). Important terms from mineralogy, geology, metallurgy, electrical engineering, computer technology, nuclear engineering, agriculture, botany, medicine, zoology, physics, and mathematics are also included.

The contents of a dictionary can be investigated only by random sampling, and one looks first for terms not included in other similar works. The large majority of such tests were satisfactorily passed: in nearly all cases the dictionary gave an answer. Some reaction terms were missing, such as autoxidation, allyl rearrangement, amidolysis, protonation, as well as named reactions which present difficulties in back-transliteration since they appear phonetically in the Cyrillic ('Uoker'-=Walker). Trouble has been taken to give as many different English meanings as possible for each Russian word. What is particularly useful is that the singular and plural forms are given at their alphabetical places for those nouns that are declined in Russian in unusual ways. It is equally useful to find a table giving the customary endings of technical words in Russian and a collection of the possible methods of declining and conjugating Russian words.

In the Foreword the author emphasizes very modestly that her dictionary, like all others, cannot be complete. But the reviewer can confirm that the terms have been selected with great care and knowledge. All those concerned with Russian technical literature will certainly find this volume of great assistance.

Christian Weiske [NB 306 IE]

Techniques of Chemistry. Vol. VII: Membranes in Separations. By *Sun-Tak Wang* and *K. Kammermeyer*. Edited by *A. Weissberger*. John Wiley and Sons, New York—London 1975. 1st Edit., xxii, 559 pp., numerous figures and tables, bound, £ 17.50.

Although membranes have been the subject of scientific interest for more than a century, intensive research and development was not undertaken until a few years ago when it became apparent that they could be employed for large scale separations of molecular mixtures. Current interest in membranes and membrane separation processes has become so diversified that the voluminous literature is widely scattered in specialized journals and terminology tends to be inconsistent.

By compiling a comprehensive description of all currently known membrane separation processes and their applications, *Wang* and *Kammermeyer* have made a valuable contribution to this field. The need for such a work has long been recognized.

The first chapters present fundamental definitions and descriptions of membranes and membrane transport processes. Characteristic membrane constants are defined, together with experimental methods for their determination. In subsequent chapters individual membrane processes for material separation and the essential areas of their application are briefly discussed. The book particularly emphasizes aspects of membrane processes that have an industrial application, and there are extensive and numerous examples of their use in science and industry. The methods of preparing membranes and membrane systems, however, are treated in less detail. The book gains additional current interest owing to the detailed description and discussion of commercially available membranes and membrane filter systems and a list of membrane manufacturers.

This book will be especially helpful to anyone seeking practical solutions to material separation problems by membrane processes, irrespective of whether the specific application be in medicine, or industial or pure chemistry. By bringing a a description of all membrane processes into a single volume, even the reader previously unfamiliar with the subject can quickly become familiar with the most important basic concepts, and obtain a broad overview of possible applications. The more scientifically oriented reader interested in the theoretical aspects of membrane processes, however, will find this book of more limited value.

Heiner Strathmann [NB 298 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Basic Inorganic Chemistry. By *F. A. Cotton* and *G. Wilkinson*. John Wiley & Sons, New York 1976. viii, 579 pp., bound, $ 15.60.

Basic Chemistry. A Self-Instructional Computing Course. By *G. Beech*. Sigma Technical Press, Albrighton 1976. 83 pp., paper, £ 2.75.

Ein Gelehrtenleben. Ernst und Satire. By *E. Hückel*. Verlag Chemie, Weinheim 1975. 181 pp., bound, DM 38.00.

The Theory of Molecular Spectroscopy. Vol. 1: The Quantum Mechanics and Group Theory of Vibrating and Rotating Molecules. By *C. J. H. Schutte*. North-Holland Publishing Company, Amsterdam/American Elsevier Publishing Company, New York 1976. xvi, 512 pp., bound, $ 67.95.

Organic Synthesis by Means of Transition Metal Complexes. By *J. Tsuji*. Vol. 1 of the series "Reactivity and Structure Concepts in Organic Chemistry". Edited by *K. Hafner, J.-M. Lehn, C. W. Rees, P. v. R. Schleyer, B. M. Trost*, and *R. Zahradník*. Springer-Verlag, Berlin 1975. ix, 199 pp., bound, DM 68.00.

Alkaloide ausser Indol-, Triterpen- und Steroidalkaloiden. By *M. Hesse* and *H. O. Bernhard*. Vol. 3 of the series "Fortschritte der Massenspektrometrie". Edited by *H. Budzikiewicz*. Verlag Chemie, Weinheim 1975. xx, 372 pp., bound, DM 148.00.

Applications of Liquid Crystals. By *G. Meier, E. Sackmann*, and *J. G. Grabmaier*. Springer-Verlag, Berlin 1975. vi, 164 pp., bound, DM 56.00.

Surface Characteristics of Fibers and Textiles, Part I. Edited by *M. J. Schick*. Vol. 7 of "Fiber Science Series". Edited by *L. Rebenfeld*. Marcel Dekker, New York 1975. xii, 416 pp., bound, $ 39.50.

Lehrbuch der Elektrochemie. By *J. Koryta, J. Dvorák*, and *V. Boháčková*. Springer-Verlag, Wien 1975. xv, 348 pp., bound, DM 145.00.

Radio-Immunoassay of Steroid Hormones. Edited by *D. Gupta*. Verlag Chemie, Weinheim 1975. x, 224 pp., bound, DM 58.00.

Colloid Science, Vol. 2. Senior Reporter: *D. H. Everett*. The Chemical Society, London 1975. ix, 323 pp., bound, £ 18.00.—A volume in the series "Specialist Periodical Reports".

Topics in Current Chemistry/Fortschritte der chemischen Forschung. Edited by *F. L. Boschke*. Vol. 59: Organic Syntheses. Springer-Verlag, Berlin 1975. iv, 135 pp., bound, DM 58.00.

Topics in Current Chemistry/Fortschritte der chemischen Forschung. Edited by *F. L. Boschke*. Vol. 60: Structure of Liquids. Springer-Verlag, Berlin 1975. iv, 205 pp., bound, DM 62.00.

Kinetik der Elektrodenprozesse. By *T. Erdey-Grúz*. Akadémiai Kiadó, Budapest 1975. 581 pp., bound, DM 86.40.

Research and Development in Japan Awarded the Okochi Memorial Prize 1975. Okochi Memorial Foundation, Tokio 1975. 108 pp., paper.

Aufgabensammlung Physikalische Chemie in SI-Einheiten. By *B. W. V. Hawes* and *N. H. Davies*. Vol. 38 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1975. xi, 223 pp., paper, DM 19.80.

Organometallic Chemistry, Vol. 4. Senior Reporters: *F. G. A. Stone* and *E. W. Abel*. The Chemical Society, London 1975. xv, 497 pp., bound £ 27.00.—A volume in the series "Specialist Periodical Reports".

NMR Basic Principles and Progress/Grundlagen und Fortschritte. Edited by *P. Diehl, E. Fluck*, and *R. Kosfeld*. Vol. 10: Van der Waals Forces and Shielding Effects. Springer-Verlag, Berlin 1975. ii, 118 pp., bound DM 58.00.

Theoretical Chemistry, Vol. 2. Senior Reporters: *R. N. Dixon* and *C. Thomson*. The Chemical Society, London 1975. x, 209 pp., bound, £ 10.00.—A volume in the series "Specialist Periodical Reports".

Digital Electronics and Laboratory Computer Experiments. By *Ch. Wilkins, S. P. Perone, Ch. E. Klopfenstein, R. C. Williams*, and *D. E. Jones*. Plenum Press, New York 1975. viii, 283 pp., bound, DM 48.00.

Die Mössbauer-Spektroskopie als Forschungsmethode in der angewandten organischen Chemie. Stand und Perspektive. By *D. Christov, Z. Bontschev*, and *Z. Busova*. Bulgarian Academy of Sciences, Sofia 1974. 86 pp., bound.

Electrochemistry, Vol. 5. Senior Reporter: *A. R. Thirsk*. The Chemical Society, London 1975. viii, 311 pp., bound, £ 17.00.—A volume in the series "Specialist Periodical Reports".

Allgemeine und Anorganische Chemie. By *V. Gutmann* and *E. Hengge*. Verlag Chemie, Weinheim 1975. 2nd revised and enlarged edition. xi, 397 pp., paper, DM 39.00.

Evaluated Kinetic Data on Gas Phase Hydrogen Transfer Reactions of Methyl Radicals. By *J. A. Kerr* and *M. J. Parsonage*. Butterworths, London 1976. 286 pp., bound, £ 18.00.

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Nitrogen as Leaving Group: Aliphatic Diazonium Ions

By Wolfgang Kirmse[*]

Nitrogen is one of the best known leaving groups. Decomposition of aliphatic diazonium ions has rendered carbocations (carbon cations) accessible in cases where the solvolysis of halides or sulfonic esters follows different pathways. The limits of unassisted decomposition are seen in primary diazonium ions, where the participation of external nucleophiles and of neighboring groups in the elimination of nitrogen becomes noticeable. Cyclopropanediazonium ions occupy a position intermediate between aliphatic and aromatic diazonium ions. New versatile methods of generating aliphatic diazonium ions facilitate their preparative use.

1. Introduction

The pronounced stability and ready formation of molecular nitrogen have rendered numerous reactive intermediates of organic chemistry accessible by elimination of nitrogen. Diazeniates *(1)* afford carbanions in a step of the Wolff-Kishner reduction and related reactions[1]. Azo compounds *(2)* generate radicals; for instance, the readily accessible compound azoisobutyronitrile is frequently employed as an initiator of radical chain reactions[2]. Thermal or photochemical decomposition of diazo compounds *(3)* is indispensable for the generation of carbenes[3], and the decomposition of diazonium ions *(4)* often leads to carbocations (carbon cations)[4–7].

$$R{-}N{=}N{:}^{\ominus} \longrightarrow R{:}^{\ominus} + N_2 \quad (1)$$

$$R{-}N{=}N{-}R \longrightarrow 2\,R\bullet + N_2 \quad (2)$$

$$R_2C{=}N_2 \longrightarrow R_2C{:} + N_2 \quad (3)$$

$$R{-}\overset{\oplus}{N}{\equiv}N \longrightarrow R^{\oplus} + N_2 \quad (4)$$

The reactions of aliphatic diazonium ions and the way in which nitrogen differs from other leaving groups will be discussed in the present article.

The differences in stability between aromatic and aliphatic diazonium ions are impressive. Since their discovery by *Griess*[8], aromatic diazonium ions have found wide application in the synthesis of intermediates and dyes[9]. Some vinylic diazonium salts are also isolable[10]. But all we find about aliphatic diazonium salts in many textbooks is that they "spontaneously" decompose. The far greater ease with which the diazonium nitrogen is released from an sp^3 carbon as compared with an sp^2(aryl)carbon atom can be explained by several factors:

a) Aromatic diazonium ions are stabilized by interaction between the π-systems of the ring and the diazonium group. This effect is difficult to assess quantitatively. The thermodynamic data of the isoelectronic but uncharged nitriles indicate a stabilization of Ar—CN relative to R—CN of about 15 kcal/mol.

b) The high energy of aryl cations impedes the expulsion of nitrogen from aromatic diazonium ions. If the ionization potentials of the corresponding radicals are adopted as a measure for the stability of cations, then the phenyl cation assumes a position intermediate between the methyl and the ethyl cation[11]. A similar result is obtained from the heat of reaction of the hypothetical heterolysis

$$R{-}H \rightarrow R^{\oplus} \cdot H^{\ominus}$$

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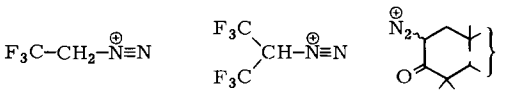
which is 314 kcal/mol for methane, 303 kcal/mol for benzene, and 280 kcal/mol for ethane[12]. (All these data apply to the gas phase.)

The few aliphatic diazonium ions that are detectable by spectroscopy, such as the 2,2,2-trifluoroethanediazonium ion *(5)*[13], the hexafluoropropane-2-diazonium ion *(6)*[14], and 2-oxocyclohexanediazonium ions *(7)*[15] bear powerfully electron-withdrawing substituents which destabilize the corresponding carbocation and oppose unimolecular decomposition.

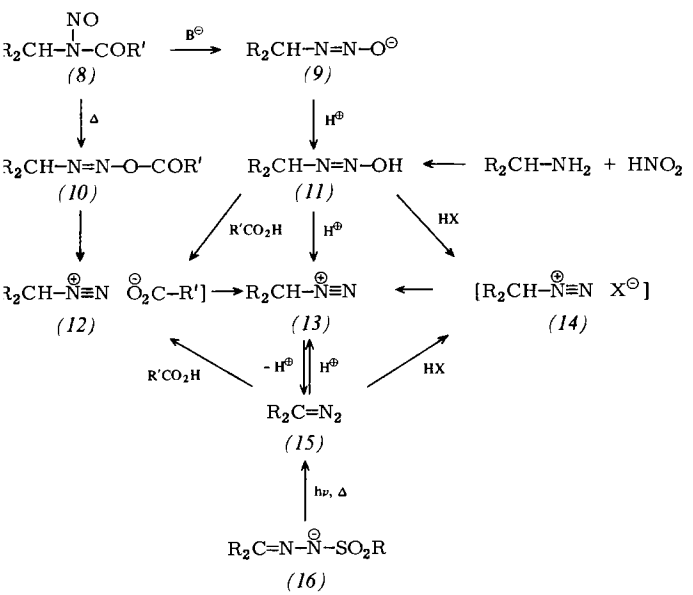


(5) *(6)* *(7)*

c) The difficult nature of bimolecular substitution of arenes stabilizes arenediazonium ions relative to their aliphatic analogs. Careful application of all the usual mechanistic criteria has confirmed that the decomposition of benzenediazonium ions leads to phenyl cations[16]. Methanediazonium ions are likewise stable in the gas phase (their decomposition to methyl cation and nitrogen is endothermic to the extent of 38 kcal/mol)[17], but not in solution. It seems an obvious conclusion that some aliphatic diazonium ions react with nucleophilic participation of solvent (cf. Section 4.1), especially when unimolecular decomposition would lead to a high-energy carbocation. This competition pathway is not open to aromatic diazonium ions.

2. Formation of Aliphatic Diazonium Ions

The most important pathways leading to aliphatic diazonium ions *(13)* are sketched out in Scheme 1.



Scheme 1

2.1. Nitrosation (Diazotization) of Primary Amines[18]

Amines are usually treated with nitrous acid (sodium nitrite) in acidic aqueous solution or glacial acetic acid. Reaction has to be performed in a relatively narrow pH range (pH 3–5 for alkylamines) since both the free amine and free nitrous acid must be present. The kinetics of nitrosation are usually complex; rates given by

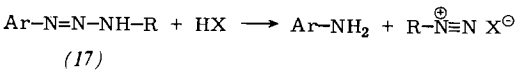
$$v = k[RNH_2][HNO_2]^2 \text{ and } v = k[RNH_2][HNO_2][H^+]$$

have been observed in limiting cases. In the former case N_2O_3 is regarded as the nitrosation reagent, and $H_2NO_2^+$ or NO^+ in the latter[18]. With long-chain amines the rate of nitrosation increases in the range of micelle formation[19].

A suitable reagent for diazotizations in weakly alkaline aqueous solutions is disodium pentacyanonitrosylferrate ("sodium nitroprusside") which transfers its nitroso group to amines at pH 9–11 but decomposes at higher pH values[20]. Nitrosation in aprotic solvents can be accomplished by reaction of the amine with an alkyl nitrite in the presence of one equivalent of acid[21]. Although it is more appropriate to speak of proton-deficient rather than aprotic solutions, product formation is influenced considerably by this variant of diazotization. Similar observations have been made in the reaction of amines with nitrosyl chloride[22,23] or with N_2O_4[24] in nonpolar solvents. These methods generate aliphatic diazonium ions in the form of ion pairs.

2.2. Acid Cleavage of Triazenes

3-Alkyl-1-aryltriazenes *(17)*, which are formed by azo coupling of aromatic diazonium ions with aliphatic amines, decompose into aliphatic diazonium ions and aromatic amines on acid catalysis[25]. The resulting diazonium ions react both with the anion of the acid and with the liberated amine[26]. On use of silica gel as "acid", the amine becomes the sole co-reactant[27].



(17)

2.3. Thermolysis of *N*-Nitrosoamides[28]

The slow preliminary step of the thermolysis of an *N*-nitrosoamide *(8)* (Scheme 1) consists in rearrangement to a diazo ester *(10)*. Aliphatic diazo esters decompose by a polar mechanism *via* diazonium-carboxylate ion pairs *(12)* whose fate largely depends upon the solvent. Whereas the thermolysis of *N*-nitrosoamides, nitrosation of primary amines, and protonation of diazoalkanes (cf. Section 2.5) lead to similar results in polar solvents, diazo esters furnish mainly products of ion pair recombination in nonpolar media; subsequent reactions (*e.g.* rearrangements) are suppressed[28,29].

2.4. Alkali Cleavage of *N*-Nitrosoamides

The initial step of alkali cleavage of *N*-nitrosoamides *(8)* (Scheme 1) is the removal of the acyl group by a base, forming alkanediazotates *(9)*. Bases attack the carbonyl group of *N*-nitrosoamides *(8)*, R′ = alkyl or aryl, and *N*-nitrosocarbamates *(8)*, R′ = OR″[30–32], but an N—H bond of *N*-nitrosoureas with elimination of cyanate[33,34]. The alkanediazotates *(9)* can be isolated from aprotic solvents in the form of their alkali metal salts[35–38]; they have a *Z* configuration[36]. In

protic solvents rapid protonation usually ensues to form the diazo hydroxide *(11)* and diazonium ion *(13)*; however, the diazotate intermediate can also be trapped intramolecularly by oxirane[39], allene[40], and alkyne functions[41].

Decomposition of the diazo hydroxide *(11)* in an ion pair process can afford alcohols. Evidence was obtained for such a course on hydrolysis of 2-octanediazotate with ^{18}O-labeled water[42] and on alcoholysis of 1-phenylethanediazotate[43, 44]. Viewed quantitatively this pathway is of minimal significance. The most important branching point of the reaction is the alkanediazonium ion *(13)*, which can undergo not only decomposition and substitution reactions but also deprotonation to give the diazo compound *(15)*. Insofar as this process is reversible[33], alkali cleavage of *N*-nitrosoamides here merges with the protonation of diazoalkanes (Section 2.5).

2.5. Protonation of Diazoalkanes[45]

The sensitivity of diazo compounds *(15)* to acids (Scheme 1) is very dependent upon substituents. While diazoalkanes are even protonated in alkaline solution, diazo ketones, diazo esters, and diazo sulfones only react at low pH values. Cases are known of rate-determining proton transfer (which is slow compared with the subsequent reactions of the diazonium ion), as are examples in which a reversible diazo-diazonium equilibrium precedes diazonium decomposition. These cases can be distinguished by H-D exchange experiments and solvent isotope effects. Which mechanism predominates depends upon the structure, but also on the pH value. Primary diazo ketones ($RCO—CHN_2$)[46], diazo esters ($N_2CH—CO_2R$)[47], and diazo sulfones ($RSO_2—CHN_2$)[48] display predecomposition equilibria, whereas secondary diazo ketones ($RCO—CR'N_2$)[49] and diazo esters ($N_2CR—CO_2R'$)[50], like diphenyldiazomethane[51, 52], undergo rate-determining protonation. 1-Diazobutane exhibits irreversible protonation in acidic solution, but reversible protonation in alkaline solution[53].

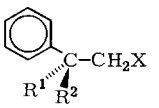
A convenient method of generating diazonium ions in alkaline solution is photolysis of sulfonyl hydrazones or their anions *(16)* (Scheme 1). In this photochemical variant of the Bamford-Stevens reaction[54], initial elimination of sulfinate gives the diazo compound *(15)*[55] which is then protonated by solvent. With secondary diazo compounds (R_2CN_2, R = alkyl) in particular, protonation at room temperature is fast compared with photochemical or thermal decomposition so that the reaction products of carbenes occur in only small amounts, if at all.

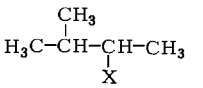
Reaction of diazoalkanes with acids in nonpolar solvents leads to ion pairs[29, 52, 56, 57], like the thermolysis of *N*-nitrosoamides (Section 2.3).

3. Carbocations as Intermediates of Diazonium Decomposition

3.1. "Hot" Cations?

Identical intermediates give identical products. According to this criterion, the carbocations generated in different ways are not identical, since the product distribution usually depends upon the genesis of those species. Admittedly, cases are known where the S_N1 reactions of halides or sulfonic esters and decomposition of diazonium ions lead to corresponding results, and a common intermediate appears to be proven[58, 59]; generally speaking, however, the intermediates of diazonium decomposition are more prone to rearrangement and are less selective than those of S_N1 solvolyses. For instance, the deamination of 2-arylalkylamines *(18)* is accompanied by competing 1,2-shifts of all groups (aryl, alkyl, hydrogen) attached to the β-C atom[60–62]. Only the aryl group migrates in the solvolysis of corresponding sulfonic esters *(19)*[62, 63].





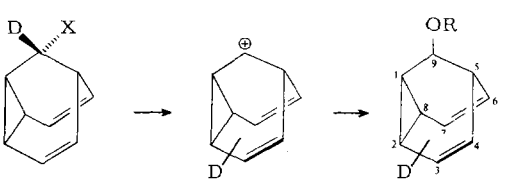
(18), X = NH_2
(19), X = OSO_2R
R^1, R^2 = Alkyl, H

(20), X = NH_2
(21), X = OSO_2-C_6H_4-CH_3 (*p*)

Similarly, deamination of 3-methyl-2-butylamine *(20)* involves not only a hydrogen shift but also a methyl shift (although the latter, as a "degenerate" rearrangement, does not lead to any gain in energy and can only be detected by isotopic labeling)[64]. Solvolysis of the *p*-toluenesulfonate *(21)* proceeds almost exclusively with H shift[65].

The reason for this and similar findings[4, 5] is no doubt to be found in the lower activation energy of the (exothermic) decomposition of diazonium compounds compared to that for compounds having poorer leaving groups. It is a matter of dispute just how these differences in the ionization step affect product formation. According to *Young*[66], elimination of nitrogen from aliphatic diazonium ions should lead to high-energy, "hot" carbocations. This hypothesis constantly recurs in various forms right up to the very latest publications, although its original foundation—product ratios in the substitution of allyldiazonium ions—has since collapsed (cf. Section 4.1).

The term "hot" carbocation means an intermediate still possessing excess energy arising from its exothermic mode of formation and not in thermal equilibrium with its environment. Transformation of heat of reaction into excitation energy of a product ("chemical activation") is well known for gas phase reactions[67], but there are no unequivocal examples of such reactions occurring in solution[68]. The following test for excess energy in intermediates of diazonium decomposition has recently been reported[69]: On solvolysis of tricyclo[3.3.1.$0^{2,8}$]nona-3,6-dien-9-yl ("barbaralyl") toluenesulfonate a D label on C-9 is initially distributed over positions 3, 7, and 9. In less nucleophilic media and after repeated formation of the barbaralyl cation the label is scrambled over all positions[70]. The barbaralyl cation accordingly experiences two distinct degenerate rearrangements which differ only slightly in their activation energies (for mechanism see

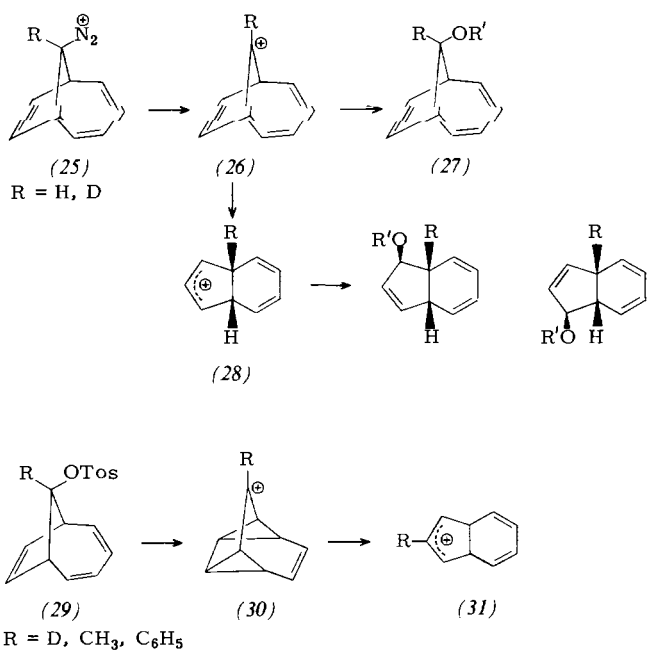


(22), X = OTos
(23), X = $N_2^{\oplus}$

(24)

ref. [70]). If decomposition of the barbaralanediazonium ion *(23)* were to give a cation *(24)* having excess energy then the redistribution of the deuterium would be more extensive than that observed on solvolysis. However, the distribution of deuterium was found to depend solely upon the solvent nucleophilicity and not upon the mode of formation of the cation *(24)*[69]. Thus solvolysis and diazonium decomposition generate the same ("cold") barbaralyl cation.

In the light of such findings, use of the rather confusing term "hot" in connection with the intermediates of diazonium decomposition should be abandoned. Of more significance than *energy* differences are differences in the *structure* of transition states and intermediates of the various cation-forming reactions. The facile process of diazonium decomposition requires far less assistance from neighboring groups or external nucleophiles than the dissociation of halides or sulfonic esters. The above differences in behavior of *(18)/(19)* and *(20)/(21)* can be rationalized in this way. *Skell*[4] therefore describes the intermediates of diazonium decomposition as "free" cations, while poorer leaving groups afford "encumbered" cations. But this mode of expression places too much emphasis on the influence of external factors (gegenion, co-reactant). It is often precisely intramolecular effects (neighboring group participation) which account for the differences between deamination and solvolysis, as exemplified in Scheme 2.



Scheme 2

Decomposition of bicyclo[4.2.1]nona-2,4,7-triene-9-diazonium ions *(25)* leads to the cation *(26)* which is partly trapped by substitution to give *(27)* and partly transformed by an alkyl shift into the 3a,7a-dihydroindenyl cation *(28)*. A substituent at position 9 of *(25)* expectedly reappears at the bridgehead of the dihydroindene skeleton[69]. Solvolysis of the toluenesulfonate *(29)* does not afford *(27)*; the only products obtained are dihydroindene derivatives bearing the substituent R at position 2, being derived from the cation *(31)*[71, 72]. Formation of this cation, an isomer of *(28)*, is explained with the aid of the intermediate *(30)*, *i.e.* by intramolecular Diels-Alder reaction. Whether this diene reaction occurs before ionization or simultaneously has yet to be decided, but in any case it leads to a stabilized dicyclopropylcarbenium ion *(30)*. Formation of *(26)* is possible only because of the excellent leaving group nitrogen.

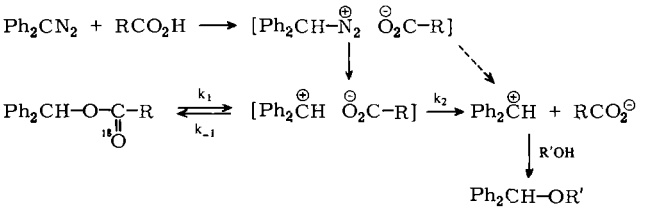
The pair of compounds *(25)/(29)* provides an impressive example for the production of "free" carbocations by diazonium decomposition. Nevertheless, only few diazonium ions react in manners completely independent of their environment. The "limits of freedom" are critically examined in the following sections.

3.2. Ion Pairs

In media of low polarity, the reactions of aliphatic diazonium ions will be influenced by the spatial proximity of the gegenion. The following observations are rationalized by the occurrence of ion pairs.

3.2.1. Product Ratios

Reaction of diphenyldiazomethane with carboxylic acids in ethanol yields a greater proportion of benzhydryl esters (60—70 %) than would be expected from the modest nucleophilic character of the carboxylate ion[45]. The product ratio depends only little on the nature of the acid[52] and remains unchanged on addition of its salts. It appears likely that the benzhydryl esters arise from diazonium-carboxylate ion pairs, whereas benzhydryl ethers are formed from the dissociated diazonium ions or the carbenium ions (Scheme 3). Comparison with the solvolysis of benzhydryl esters supports this concept. (internal return from the ion pair is measured by the distribution of ^{18}O): similar values of k_{-1}/k_2 are found for both reactions[73].



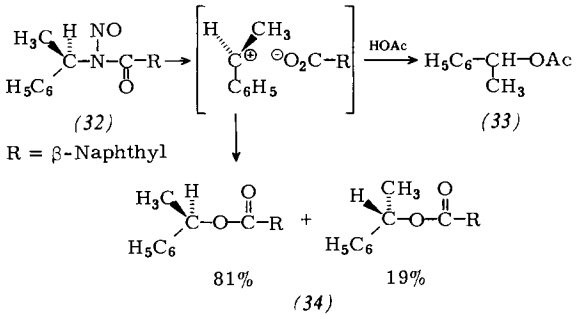
Scheme 3

Both 1-diazo-2-butene and 3-diazo-1-butene afford the corresponding ester without allylic rearrangement on treatment with 3,5-dinitrobenzoic acid in ether, while identical mixtures of the isomeric butenols are obtained in aqueous perchloric acid[45]. The formation of *sec*- and *tert*-butyl derivatives on thermolysis of *N*-isobutyl-*N*-nitroso-3,5-dinitrobenzamide increases with increasing solvent polarity[74]; a similar trend occurs in *n*-propyl→isopropyl rearrangements[29]. In the thermolysis of *N*-nitrosoamides, ion-pair orientation can reach such an extent that complete equilibration of the carboxylate oxygen atoms even becomes impossible[75].

3.2.2. Stereochemistry

Substitution of the diazonium nitrogen in polar media occurs with racemization and inversion (cf. Sections 3.3 and 4.1). In ion-pair processes, however, the configuration is largely retained. Decomposition of the optically active *N*-nitrosoamide *(32)* in the presence of acetic acid gives the "ion-pair product" *(34)* exhibiting 81% retention (19% inversion); the

acetate *(33)* which is also formed in the reaction is largely racemic[29, 75]. Extensive retention can also be achieved by reaction of the hydrochlorides of optically active amines with pentyl nitrite in benzene or light petroleum[76]. Even the nitrosation of aliphatic amines in aqueous acetic acid displays a transition from inversion to retention as the concentration of acetic acid increases, indicating formation of diazonium-acetate ion pairs[19, 77–80].



(32) *(33)* *(34)*

R = β-Naphthyl

The question whether ion-pair effects are operative only in direct substitution or also at the origin of rearrangements has still to be settled. A particular source of disagreement is whether the stereochemical preferences of bicyclic cations ("memory effects") are due to conformational barriers, delocalized bonds, or ion pairs[81, 82].

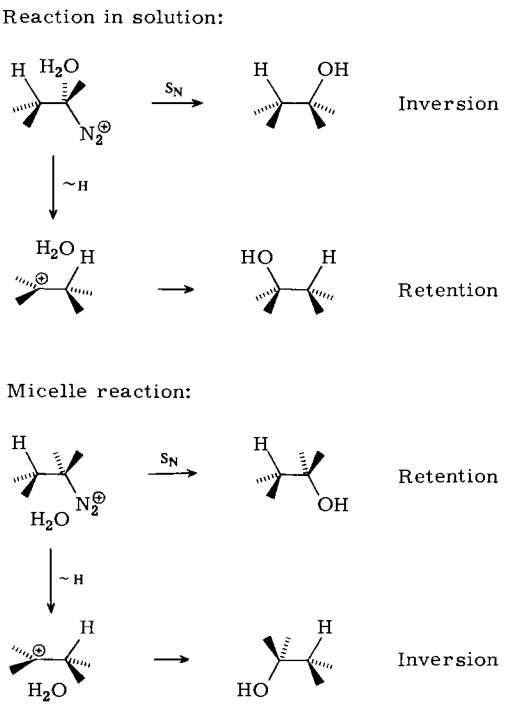
3.3. Micelle Effects

Under the conditions of diazotization with nitrous acid (pH 3—5) alkylamines exist mainly as alkylammonium ions. On exceeding a critical micelle concentration (cmc), the alkylammonium ions begin aggregating to micelles. The hydrophobic alkyl groups point to the interior of the micelles, while the polar ammonium groups are oriented on the surface[83]. Acid-base equilibration between free amine and ammonium ions is fast compared with mass transfer between the micelle and solution. Hence above the cmc, diazotization and diazonium decomposition also partly occur within the micelles. This has an effect on the product distribution and stereochemistry[19, 84]: in solution substitution of the diazonium nitrogen proceeds with partial inversion (and racemization). Micelle formation impedes back-side attack by the solvent; thus the inversion decreases with increasing concentration until retention is finally observed[19]. A linear relationship exists between the micelle content of the solution

$$F_m = (c_i - \text{cmc})/c_i$$

(c_i = initial amine concentration) and the stereochemistry of the product; this demonstrates that the overall reaction is made up of a solution component and a micellar component[19]. The stereochemistry of the products of 1,2-hydrogen shifts also depends upon micelle formation[84]. Since the migrating hydrogen assumes an antiplanar position relative to the leaving group[64, 85] it is replaced with retention in dilute solution and with inversion in the micelle (Scheme 4).

Furthermore, the lower effective concentration of water in the micelle also favors increased elimination and rearrangement at the expense of direct substitution[84]. The structure of the micelles and hence the course of micellar reactions depends upon the gegenion; the above effects are especially pronounced for poorly hydrated ions such as ClO_4^- and BF_4^- which favor dense micelle packing[19].



Scheme 4

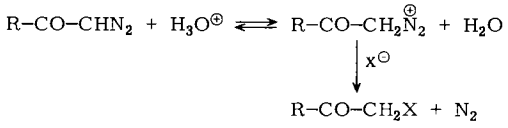
4. Participation of Nucleophiles in Diazonium Decomposition

4.1. Intermolecular Reactions

The product-determining step can be studied by kinetic methods only for stable diazonium ions and diazo-diazonium equilibria. Bis(trifluoromethyl)diazomethane *(35)* is completely protonated in fluorosulfuric acid at −70 °C. Decomposition of the diazonium ion *(6)* at −5 to +5 °C obeys second-order kinetics [first order in *(6)* and first order in fluorosulfate][14]. Since *(6)* would afford an extremely unstable cation by unimolecular decomposition it even reacts with the weak nucleophile fluorosulfate according to an S_N2 substitution.

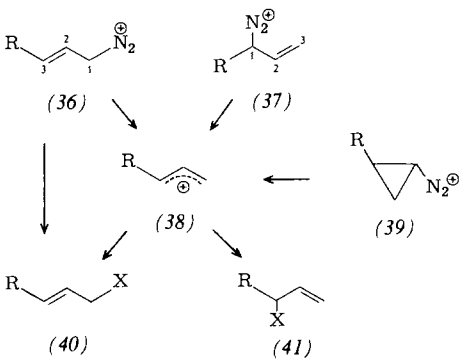
$$\underset{(35)}{(CF_3)_2CN_2} + FSO_3H \longrightarrow \underset{(6)}{(CF_3)_2CH\text{–}\overset{\oplus}{N}_2\ {}^{\ominus}OSO_2F} \xrightarrow{k_2} (CF_3)_2CH\text{–}OSO_2F + N_2$$

The rate of decomposition of diazoacetic ester[47, 86] and of diazoacetone[87] in acid solution depends not only upon the acid strength (Hammet acidity function H_0) but also upon the acid anion. With chloride, bromide, and iodide a linear relationship is obtained between $\log k$ and the nucleophilicity parameters n of *Swain* and *Scott*[88] ($\log k_x/k_{H_2O} = n \cdot s$; $s = 0.43$ for diazoacetic ester and $s = 0.36$ for diazoacetone). The kinetic data are a convincing argument for participation of nucleophilic anions—and even of water—in the decomposition of primary oxodiazonium ions (Scheme 5).



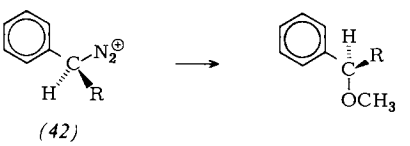
Scheme 5

Secondary diazoketones cannot be studied by this method because the protonation is rate determining (Section 2.5). However, the product distributions obtained in competition reactions also permit derivation of reaction parameters of the Swain-Scott type ($s = 0.37$ for 3-diazo-2-butanone; $s = 0.33$ for 1-diazo-1-phenylacetone)[89]. The good agreement of these parameters and those obtained above suggest the occurrence of S_N2 substitution even with secondary oxodiazonium ions.



Product analysis also throws some light on the reactions of allyldiazonium ions. This is a classical problem of diazonium decomposition which led to the hypothesis of "hot" cations (Section 3.1). If 1- and 3-substituted allyldiazonium ions react *via* an allyl cation as common intermediate then they should give identical mixtures of products. However, product mixtures are usually obtained in which the structure of the starting material predominates[66]. In order to draw the correct conclusions from these results it must be known in what ratio the delocalized allyl cation *(38)* forms the two isomeric allyl derivatives *(40)* and *(41)*. This important fact is obtained from ring opening of the cyclopropanediazonium ion *(39)*. Falsification of the product ratios by direct substitution is impossible in this case. The dependence of the product ratio upon the base concentration (*e.g.* methoxide in methanol) was employed as a further criterion. The species *(38)* should yield *(40)* and *(41)* in a constant ratio, whereas a direct substitution in *(36)* or *(37)* should be favored by the strongly nucleophilic methoxide. Series of experiments with $R = C_6H_5$[90], CH_3[91], $C(CH_3)_3$[92], and D[93] showed that the ratio of products *(40)* and *(41)* obtained from *(37)* and *(39)* is independent of base and approximately constant. Thus it is established that secondary allyldiazonium ions of type *(37)* largely react *via (38)* as intermediate. On starting with *(36)* the ratio *(40)*/*(41)* was much higher and increased with increasing base concentration. Participation of the nucleophile in nitrogen elimination accordingly appears likely in primary allyldiazonium ions such as *(36)*; its significance increases with decreasing stabilization of the allyl cation *(38)* ($R = C_6H_5 < CH_3 < C(CH_3)_3 < D$)[93].

Similar conclusions are drawn from the stereochemistry of substitution in benzyldiazonium ions *(42)* (Table 1). In 1-phenylethanediazonium ions ($R = CH_3$) the extent of inversion is independent of the base concentration[44] (pure S_N1 mechanism), while in deuterated α-toluenediazonium ions a slight increase in inversion suggests incipient participation of the nucleophile[94]. Unfortunately, the stereochemistry of alkanediazonium ions cannot be studied in alkaline solution since the diazo-diazonium equilibrium (see Sections 2.4 and 2.5, and Scheme 1) then leads to racemization. It should be pointed out, however, that deamination of optically active [1-D_1]-butylamine with nitrous acid is accompanied by 68% inversion[95], whereas secondary amines display only 20 to 25% inversion[19].



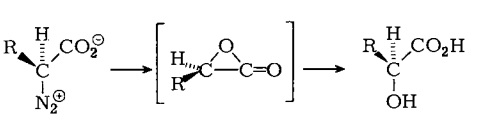
(42)

Table 1. Methanolysis of the 1-phenylethanediazonium ion *(42)*, $R = CH_3$, and the [α-D]-toluenediazonium ion *(42)*, R = D.

Base	$R = CH_3$	R = D
	Inversion [%]	
$CH_3OH/NaHCO_3$	20.6	26
CH_3OH/Na_2CO_3	20.4	32
CH_3OH/0.1 N $NaOCH_3$	19.6	40
CH_3OH/1 N $NaOCH_3$	18.6	42
CH_3OH/3 N $NaOCH_3$	20.6	

4.2. Neighboring Group Effects

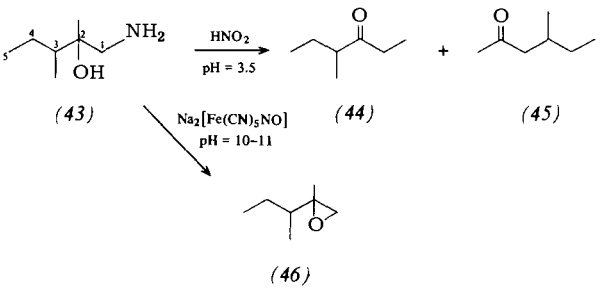
The effect of a nucleophile is often enhanced if it is located in the same molecule in the proximity of the leaving group. At least one neighboring group effect has long been known to occur in diazonium ions: diazotization of α-amino acids affords α-hydroxy acids with retention of configuration (Scheme 6)[96, 97]. The stereospecificity (*ca.* 95%) can be determined particularly easily from the formation of diastereomeric products from isoleucine[98]. The stereochemical findings are explained by double inversion: intramolecular substitution of the diazonium group by carboxylate leads to an α-lactone which is opened by water in a back-side attack. If the diazonium group is located on a tertiary C atom then neighboring carboxylate can no longer hinder formation of a carbocation; the stereospecificity falls to *ca.* 30% retention[99].



Scheme 6

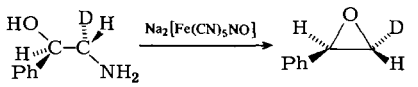
The alkoxide function can also act as a neighboring group, albeit only in primary diazonium ions. Deamination of 1-amino-2,3-dimethylpentanol *(43)* proceeds like a pinacol rearrangement in acid solution to give the ketones *(44)* (methyl shift) and *(45)* (*sec*-butyl shift). Diazotization in alkaline solution, however, gives exclusively the oxirane *(46)*[100]. As shown by the example of the amino alcohol *(47)*, the diazonium nitrogen is displaced with inversion on oxirane formation[101]. If the leaving group is attached to a secondary C atom, how-

ever, then the pinacol rearrangement cannot be avoided by working in an alkaline medium[98, 101]. Exceptions to this rule are encountered with conformationally rigid systems in which the relative position of the leaving and neighboring groups is fixed[102].



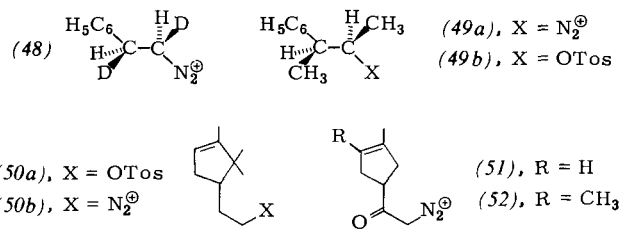
(43) (44) (45)

(46)



(47)

The reactions of the 2-phenylethanediazenium ion *(48)* can be analyzed by ^{14}C- and D-labeling[103, 104]. Migration of the phenyl group in *(48)* proceeds with complete inversion[104]. Far less stereospecificity is shown by the 3-phenylbutane-2-diazonium ion *(49a)*[105a] (leaving group on a secondary C atom), in contrast to the toluenesulfonate *(49b)* which reacts in a highly stereospecific manner[105b]. Similar differences are found between the toluenesulfonate *(50a)*, which like numerous 2-(3-cyclopentenyl)ethyl toluenesulfonates[106] reacts completely with double-bond participation to give norbornane derivatives, whereas the diazonium ion *(50b)* furnishes only 15–20 % bicyclic products[107]. If the alkanediazonium group in *(50b)* is replaced by the more reluctantly decomposing oxodiazonium function (cf. Section 4.1) then the yield of norbornane derivatives rises to 90 % in the case of *(51)* and 100 % with *(52)*[108].

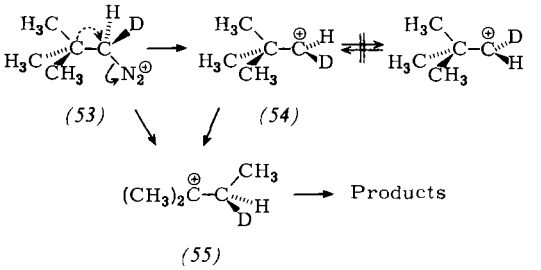


(48) (49a), X = $N_2^{\oplus}$ (49b), X = OTos

(50a), X = OTos (50b), X = $N_2^{\oplus}$ (51), R = H (52), R = CH_3

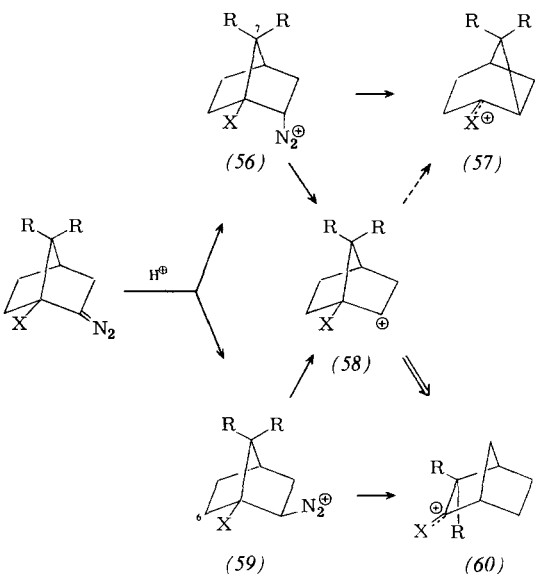
Stereochemical studies and product analyses can only hint at the occurrence of neighboring group effects. Since kinetic data are generally not available for diazonium decomposition, alternative interpretations cannot be definitely ruled out—*e.g.* very short-lived intermediate cations showing no (or only incomplete) rotation about C—C bonds. Decomposition of the optically active [1-D_1]-neopentanediazonium ion *(53)* affords products derived from *(55)* with 85% inversion[109]. This result is compatible with both a synchronous reaction of *(53)* and a very short lifetime of the primary cation *(54)*.

The behavior of norbornanediazonium ions permits a clearer distinction between these alternatives. In the *exo*-diazonium ion *(59)*, C-6 is suitably oriented for participation



(53) (54) (55)

in elimination of nitrogen; a synchronous reaction leads to the norbornane derivative *(60)*. X is a cation-stabilizing substituent (OR, NHR, *etc.*), which prevents further rearrangements. In the *endo*-diazonium ion *(56)* steric constraints merely permit participation of C-7 in nitrogen elimination; the rearrangement leads into the bicyclo[3.1.1]heptane series *(57)*. In principle both rearrangements are available to the norbornyl cation *(58)* as a possible intermediate; however, it preferably forms the less strained norbornane derivative *(60)*. In favorable cases (X = NH_2, R = CH_3) almost complete rearrangement to *(57)* is observed; the ratio *(57)*/*(60)* increases with increasing donor character of X and R[110]. These results strongly suggest



(56) (57) (58) (59) (60)

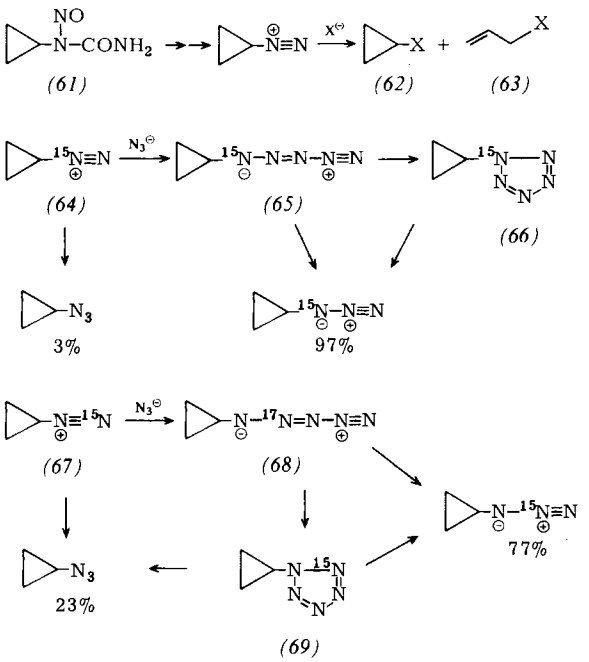
a synchronous reaction of the *endo*-diazonium ion *(56)*. Acceptor substituents in position 3 have a similar but less pronounced effect[111, 112].

5. Cyclopropanediazonium Ions

5.1. Azo Coupling

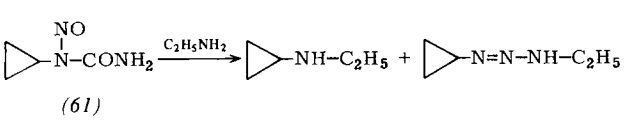
In weakly nucleophilic media, cyclopropanediazonium ions predominantly give allyl derivatives such as *(63)*. In the presence of strong nucleophiles cyclopropane derivatives of type *(62)* are also obtained; alkaline cleavage of *N*-cyclopropyl-*N*-nitrosourea *(61)* provides almost ideal conditions for this reaction[113]. While iodide ions give *(62)* and *(63)* (X = I) in the ratio 0.2 : 1, the ratio of the azides formed *(62)*/*(63)* (X = N_3) in the presence of azide ions is about 15 : 1. These drastic differences suggest that azide reacts *via* a mechanism not open to iodide. Starting from the [1-^{15}N]-labeled cyclopropanediazonium ion *(64)*, 97 % of the label reappears in the

cyclopropyl azide; it is formed almost exclusively by azo coupling and subsequent decomposition of the pentazene *(65)* and/or the pentazole *(66)*[114]. In contrast, the cyclopropyl azide formed from the [2-^{15}N]-labeled diazonium ion *(67)* contains only 77 % of the ^{15}N[114, 115]. Comparison with *(64)* indicates reaction branching at the pentazene *(68)*, which



partly (60 %) decomposes directly and partly (40 %) cyclizes to pentazole *(69)*. Compound *(69)* gives equal amounts of labeled and unlabeled cyclopropyl azide. Very similar results are observed in the reaction of aromatic diazonium ions with azide[116].

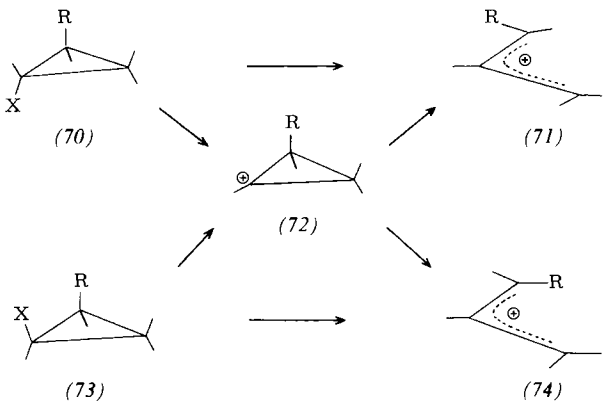
The reaction of *(61)* with ethylamine gives not only the substitution product *N*-ethylcyclopropylamine but also the coupling product 3-ethyl-1-cyclopropyltriazene (30%)[115, 117]. Coupling of cyclopropanediazonium ions with phenols has not yet been accomplished.



Such coupling reactions show the cyclopropanediazonium ions to occupy a position intermediate between purely aliphatic and aromatic diazonium ions. The only other example known is the coupling of a bridgehead diazonium ion[118]; here, too, the hybridization of the C atom probably prevents easy elimination of nitrogen.

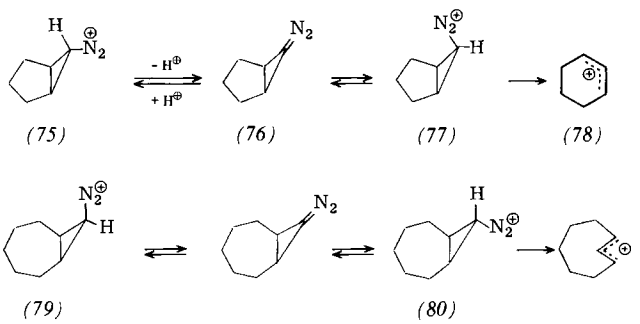
5.2. Ring Opening

One-step and multistep reaction mechanisms are conceivable for the transformation of cyclopropanediazonium ions into allyl derivatives. Does ring opening occur in a cyclopropyl cation or synchronously with elimination of nitrogen from the diazonium ion? In all cyclopropyl halides and toluenesulfonates kinetic and stereochemical criteria unequivocally support a synchronous process[119]. Substituents located *trans* to the leaving group will rotate outwards [forming a *trans*-allyl cation *(71)*] and those situated *cis* to the leaving group will turn inwards [forming a *cis*-allyl cation *(74)*][120]. Cyclo-



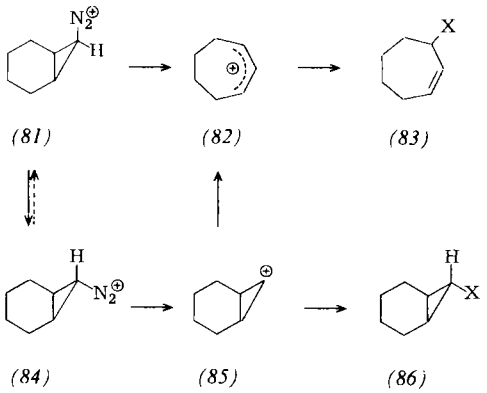
propanediazonium ions behave in a complicated way. *cis*- and *trans*-2-Phenylcyclopropane-1-diazonium ions *(73)* and *(70)*, R = C_6H_5, X = N_2^+, afford identical product mixtures, derived mainly from *(71)*, R = C_6H_5[113]. This supports a cyclopropyl cation *(72)*, R = C_6H_5, as common intermediate.

In the case of bicyclo[*n*.1.0]alkanediazonium ions, on the other hand, there are indications of a synchronous ring opening. *exo*- and *endo*-Bicyclo[3.1.0]hexane-6-diazonium ions *(75)* and *(77)* react to form cyclohexenes derived from *cis*-allyl cation *(78)*[121]. The species *(75)* only appears to contravene the Woodward-Hoffmann rules. Experiments in deuterated solvents show that the conversion *(75)*→*(78)* is accompanied by complete exchange of H-6 for deuterium, *i.e.* *(75)* initially isomerizes *via* the diazo compound *(76)* to the *endo* isomer *(77)* which can synchronously transform into *(78)*. The opposite situation is found in the bicyclo[5.1.0]octane series where the *endo*-diazonium ion *(79)* reacts with complete H/D exchange, while the *exo* isomer *(80)* give a deuterium-free product. In both cases *trans*-cyclooctene derivatives are obtained exclusively[121].



The norcarane-7-diazonium ions *(81)* and *(84)* behave in a remarkable way[122]. "Allowed" opening of the *endo*-diazonium ion *(81)* to give the cycloheptenyl cation *(82)* is only observed in acidic solution. Even in weakly alkaline media, the isomerization *(81)*→*(84)* becomes faster than the decomposition of *(81)*; norcarane and cycloheptene derivatives are then formed with complete exchange of H-7 for deuterium. The products *(83)* and *(86)* are obtained in the same ratio directly from *(84)*, then being (partly) free of deuterium, however. Accordingly, the transformation

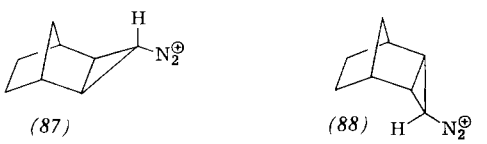
(84) → *(83)* does not proceed *via (81)* but most likely *via (85)*. Decomposition of *(84)* provides no indication for the formation of a *trans*-cycloheptenyl cation—as was obtained



(81) *(82)* *(83)*

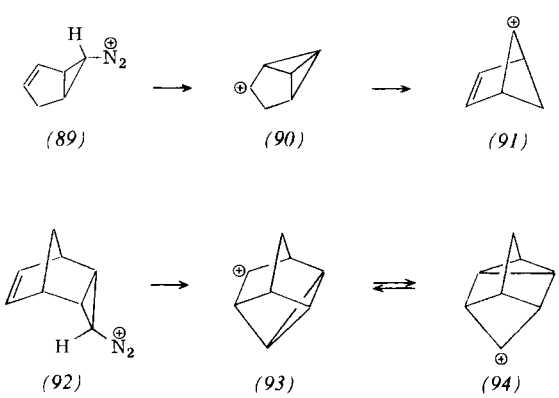
(84) *(85)* *(86)*

on solvolysis of *endo*-7-norcaryl toluenesulfonate[119]. Observations on norcarane-7-diazonium ions suggest a conformational destabilization of the *endo* isomer *(81)*. The significance of conformational effects is underlined by comparison of *(87)*, which reacts like *(75)*, and *(88)*, which behaves analogously to *(84)*[123].



(87) *(88)*

The relatively slow decomposition of some *exo*-bicycloalkanediazonium ions permits participation of double bonds. Thus *exo*-bicyclo[3.1.0]hex-2-ene-6-diazonium ions *(89)* afford products derived from tricyclo[3.1.0.$0^{2,6}$]hexyl cation *(90)* or from bicyclo[2.1.1]hex-2-en-5-yl cation *(91)*, depending on the nucleophilicity of the reactant[124]. *(92)* furnishes derivatives of the equilibrating (or mesomeric) cations *(93)* and *(94)*[125, 126]. It is essential for the success of these reactions, which provide an entry to highly strained ring systems,



(89) *(90)* *(91)*

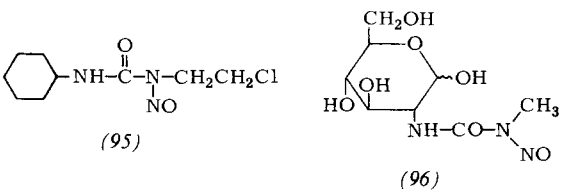
(92) *(93)* *(94)*

that the pH value lies between 7 and 8. In stronger alkaline solution isomerization yields the *endo*-diazonium ions, which then undergo (synchronous) ring opening. Rearrangement of the sensitive reaction products threatens to occur in more strongly acid solution. As in this example, preparative use of aliphatic diazonium ions is frequently a matter of optimum reaction conditions.

6. Outlook

Twenty years ago *Huisgen* summarized the latest findings in the chemistry of aliphatic diazonium ions in a excellent review[127] and greatly stimulated further development. Ion pairs were then the center of attraction; development of the ion-pair concept in the following years facilitated the interpretation of numerous, formerly incomprehensible phenomena. The discovery and application of micelle effects permitted modification of the environment of the diazonium ions in a fundamentally different way. At the same time it became increasingly clear that numerous aliphatic diazonium ions decompose with the assistance of an external or intramolecular co-reactant. *Primary* alkanediazonium ions behave like *secondary* alkyl toluenesulfonates as borderline cases between S_N1 and S_N2. As expected, the change in mechanism is shifted to less stable cations in the case of the better leaving group.

The details of diazonium decomposition possess not only theoretical and preparative interest, but also have biological implications. On the one hand, the carcinogenic and mutagenic action of nitrosamines is due to alkylation of cell components by alkanediazonium ions arising from the nitrosamines by α-oxidation and aldehyde elimination[128–130], while on the other hand cytostatics such as *N*-(2-chloroethyl)-*N'*-cyclohexyl-*N*-nitrosourea *(95)*[131] and antibiotics such as streptozotocin *(96)*[132] number among the nitrosamides and probably function by similar mechanisms.



(95) *(96)*

In vivo and *in vitro* studies have shown that heavy metal ions can intervene in this action[133]. Model experiments on the generation and decomposition of aliphatic diazonium ions in the ligand sphere of metals are still in their infancy. Perhaps they will provide new tools for modifying the leaving group properties of the nitrogen. Each addition to our knowledge about aliphatic diazonium ions will enhance their attraction as a source of carbocations and further their use in organic synthesis.

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$$\Delta H_r = \Delta H_f^0(R^{\oplus}) + \Delta H_f^0(H^{\ominus}) - \Delta H_f^0(R{-}H).$$

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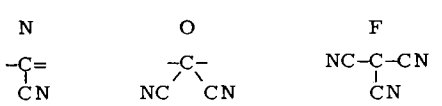
The Analogy between O and $C(CN)_2$

By Kurt Wallenfels, Klaus Friedrich, Jürgen Rieser, Werner Ertel, and Herbert K. Thieme[*]

The compounds of oxygen, *i.e.* OH acids, ethers, quinones, aldehydes, ketones, carboxylic esters and amine oxides, sulfoxides, and phosphane oxides, are compared and contrasted with those compounds which contain a $C(CN)_2$ moiety in place of the characteristic O atom. In their typical properties the pairs of analogs frequently display surprising agreement. The purpose of such analogy studies lies primarily in the estimation of reactivities; their limits are reached where specific properties of the structural components become effective.

1. The Cyano Group as a Substituent Imparting Electronegative Properties

An early attempt to characterize the behavior of atoms in an atomic assembly by a parameter was the concept of electronegativity formulated by *Pauling* in 1932[1]. This parameter affords a measure for the attraction exerted by an atom on bonding electrons. It has long been known to the organic chemist that the magnitude of this attraction depends



Scheme 1

not only on the nature of the atom itself but also on the atoms or groups of atoms to which it is bonded. One of the most powerful electronegativity-enhancing groups is the cyano group. The more CN groups a carbon atom bears, the greater will be its attraction for electrons. A kind of electronegativity series can therefore be drawn up for CN-substituted carbon atoms, resembling that of the atoms N, O, and F, and correlated with them as shown in Scheme 1.

We have developed this heuristic concept[2] in recent years, synthesizing a large number of CN-substituted compounds by analogy with those containing N and O and studying their properties. This report will compare compounds which differ solely in the presence of the $C(CN)_2$ component in place of an oxygen atom. It can be linked by double or single bonds to carbon or hydrogen, or also to nitrogen, sulfur, and phosphorus. The $C(CN)_2$ compounds are thus analogs of alcohols, ethers, quinones, aldehydes, ketones, carboxylic acids and their derivatives, and of amine oxides, sulfoxides, and phosphane oxides.

As the simplest case of an analogous reaction we shall consider the dissociation of a proton from O and from $C(CN)_2$. We see (Table 1) that the pK_a values of the $C(CN)_2$—H acids are 3.7 to 4.5 units smaller than those of the corresponding O—H acids. This difference in pK_a values is still greater in series of compounds in which two or even three oxygen atoms have been replaced by $C(CN)_2$ groups. Within a given

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series of comparable compounds, however, the same gradation of acidity is registered. Thus, as shown by *Rappoport*[7], unknown pK_a values of analogous compounds can be estimated from known pK_a values of O—H or $C(CN)_2$—H acids.

Table 1. pK_a values of O—H and $C(CN)_2$—H acids.

O—H acids	pK_a		$C(CN)_2$—H acids
H_2O	15.7 [3]	11.25 [3]	$CH_2(CN)_2$
CH_3CO—OH	4.76 [4]	1.0 [3]	CH_3CO—$C(CN)_2H$
C_6H_5—OH	9.92 [5]	5.8 [6]	C_6H_5—$C(CN)_2H$

Protonation reactions of anions of O—H acids are very fast diffusion controlled processes. Carbanions of $C(CN)_2$—H acids (malononitrile and derivatives) are protonated at a similar rate. Doubts have recently been expressed concerning the initially assumed diffusion control[8]. In any case, the high rates suggest that the pronounced C—H acidity of CN-substituted compounds are more probably due to polar field effects or inductive effects rather than to stabilization of the carbanions by electron delocalization as in the case of acidic nitroalkanes[8].

The principal application of the analogy principle is already apparent from this example: the estimation of reactivities. Analogous is by no means synonymous with identical, as becomes especially clear when specific properties of the two structural components play a particular role, *e.g.* ability of oxygen to form associates *via* hydrogen bonds with the aid of its lone pairs, or the ability of the nitrile group to stabilize an adjacent negative charge[8].

Table 2. Vertical PE ionization energies of $O/C(CN)_2$ analogs.

O compound	Vertical PE ionization energy [eV]		$C(CN)_2$ compound
H_2O	12.67 [9]	12.68 [10]	$H_2C(CN)_2$
O_2	11.55 [11]	11.78 [12, 13]	$(NC)_2C{=}C(CN)_2$
O_3	12.53 [14]	12.9 [15]	
$H_2C{=}O$	10.88 [9]	11.35 [13]	$H_2C{=}C(CN)_2$

That the two structural components do have a quantitatively similar influence in an assembly of atoms follows from a comparison of the vertical PE ionization energies (Table 2).

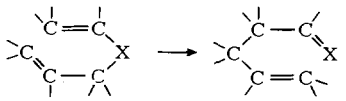
2. Ether/$C(CN)_2$ Compounds

Linkage of the $C(CN)_2$ group with two alkyl- or cycloalkyl groups affords compounds which are highly stable and chemically inert like the corresponding ethers. Reactive compounds may be expected when the structural component O or $C(CN)_2$ is incorporated into a delocalizable electron system. In such cases mainly rearrangements are observed. Classical examples are the valence tautomerism in the 7-oxanorcaradiene-oxepin *(1a)*[16] and the 7,7-norcaradienedicarbonitrile-cycloheptatriene-1,1-dicarbonitrile system[17], and the sigmatropic 3,3-shifts of the Cope and Claisen rearrangements. The thermal

(1)

(a), X = O
(b), X = $C(CN)_2$

rearrangements of allyl vinyl ether *(2a)*[18] and allylvinylmalononitrile *(2b)*[19] are entirely analogous.



(2)

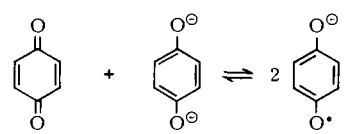
(a), X = O
(b), X = $C(CN)_2$

The decisive role of the change in electronegativity of the C atom due to substitution in the Cope rearrangement is seen in the kinetic studies by *Cope et al.* on compounds of type *(2)* with $X{=}C(CN)_2$, C(COOR)(CN), and $C(COOR)_2$[19]. The rates of these first order reactions decrease considerably along the given series.

In spite of intense effort, *Cope* was unable to carry out the classical Claisen rearrangement of aryl allyl ethers with compounds containing the $C(CN)_2$ group in place of oxygen[20]. The limitations of the analogy are again seen: it appears that the lone pairs of the oxygen in resonance with the π electrons of the aromatic ring can provide a stabilizing contribution when the low energy aromatic system is eliminated in the transition state. This is impossible in the $C(CN)_2$ "ethers".

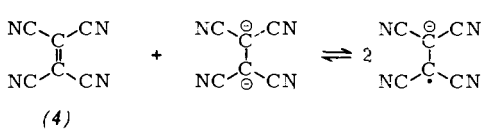
3. Quinones/Tetracyanoquinodimethanes

Both structural components are able to stabilize unpaired electrons in suitable systems. This is already apparent for oxygen from the electronic arrangement in the O_2 molecule and from the pronounced stability of the semiquinones. These radical anions arise on mixing of benzoquinone *(3)* with hydroquinone at a suitable pH value.

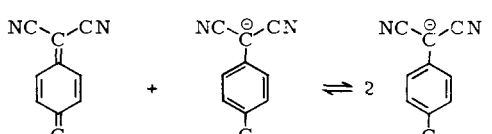


(3)

Tetracyanoethylene *(4)* accordingly reacts with the dianion of tetracyanoethane[21] and tetracyanoquinodimethane *(5)* with the dianion of tetracyano-*p*-xylene[22].



(4)

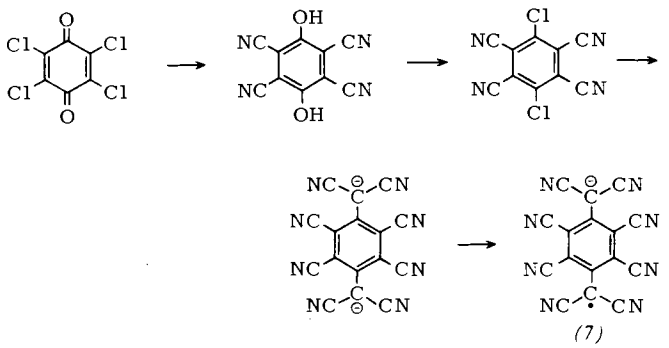


(5) *(6)*

In both cases the equilibrium lies on the side of the radical anions. The radical anion *(6)* of tetracyanoquinodimethane has recently gained great popularity because its complexes

with tetrathiafulvalene are the prototype of organic metals[23], *i.e.* organic compound with a metallic-type conductivity; they have even been ascribed superconductivity at 57 K.

In 1965 we prepared tetracyanobenzoquinone *(9)* (Table 3)[24] and pointed out its exceptional oxidizing power. Attempts have also been made to synthesize the $C(CN)_2$ analog of this quinone (Scheme 2)[25].



(7)

Scheme 2

Octacyano-*p*-xylene has so far only been prepared as the dianion (dipyridinium salt). Two polarographic waves are recorded during its anodic oxidation; they can be assigned to oxidation to the radical anion *(7)* and to octacyano-*p*-quinodimethane *(10)*, the half-wave potentials being 661 and 1290 mV respectively[25].

The radical ion *(7)* is sufficiently stable to be prepared in solution. It is obtained by oxidation of the dipyridinium salt with bromine. The completely resolved ESR spectrum affords the ^{14}N coupling constants for two sets of equivalent nuclei; $a_{N'}=1.09$ and $a_{N''}=0.125$ gauss. HMO calculations indicate a high spin density at the dicyanomethylene groups and a low spin density at the ring-bonded cyano groups[25].

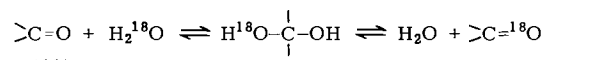
4. Carbonyl Compounds/Alkylidenemalononitriles

Two types of reactions dominate the chemistry of carbonyl compounds: In one type they are the passive partner of a nucleophilic addition at the carbonyl carbon atom. It is characterized by addition and—after subsequent elimination—substitution. In the other type initial abstraction of an α-proton transforms carbonyl compounds into the active agent of such an addition or addition-elimination reaction. As seen in Table 4, alkylidenemalononitriles fulfill nearly all expectations of this kind.

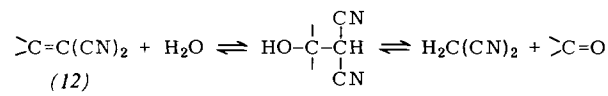
4.1. Hydration

The reversible hydration of aldehydes and ketones is one of the most thoroughly studied reactions of carbonyl compounds[42]. Both the forward and the reverse reaction can be catalyzed by acid or base. However, the nucleophilic character of water usually permits reaction without addition of catalyst. The degree of hydration is highly dependent upon structure. Thus, for instance, formaldehyde is almost completely hydrated in aqueous solution, acetaldehyde to the extent of about one half, and other aldehydes and ketones such as acetone hardly at all.

Addition of water nevertheless also occurs with these carbonyl compounds *(11)*; it is just that elimination of water from the adduct is a much faster process, as shown by studies



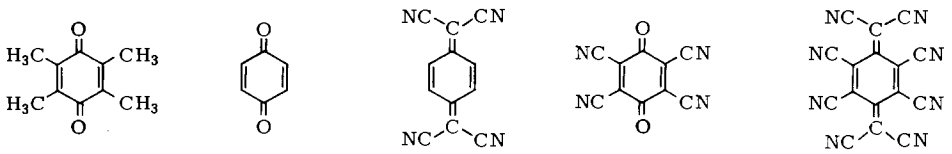
(11)



(12)

on ^{18}O-labeled water. The $C(CN)_2$ compounds *(12)* react in the same way[27, 28, 34]. Analogies in reactivity are seen to apply both to carbonyl compounds and alkylidenemalononitriles and to water and malononitrile. We have employed the reaction for preparation of aldehydes[34]; however, it is also suitable for synthesis of alkylidenemalononitriles[28].

Table 3. Polarographic data of quinones and cyano-substituted quinodimethanes [a].



(8) *(3)* *(5)* *(9)* *(10)*

	Quinone/semiquinone				Semiquinone/dianion					
	$E^1_{1/2}$ [mV]	s	C_L [mol/l]	I_1 [μA]	$E^2_{1/2}$ [mV]	s	I_2 [μA]	$\Delta E_{1/2}$ [mV]	log K	I_2/I_1
(8) [26]	− 760				−1635			875	15	
(3) [26]	− 400				−1340			940	16	
(5)	303	63	$19.3 \cdot 10^{-4}$	108	− 348	82	86	651	11	0.80
(9)	995	68	$7.57 \cdot 10^{-4}$	67	174	69	53	821	14	0.79
(10)	1209	53	$6.28 \cdot 10^{-4}$	61	661	63	56	548	9	0.92

[a] $E_{1/2}$ = half-wave potential measured *vs.* Ag/AgCl (benzonitrile) saturated with $(CH_3)_4NCl$; s = slopes of logarithmic analysis curves; C_L = molar concentration of solutions; I = normalized limiting current $I = I_d(\omega^{1/2} C_L)^{-1}$; ω = rate of revolution; K = semiquinone formation constant; $\Delta E = E^1_{1/2} - E^2_{1/2}$.

Under analogous conditions, tetracyanohydroquinone also gives the radical anion[25]. Polarographic comparison of a series of quinones with the cyano-substituted quinodimethanes is seen in Table 3. The potentials of the $C(CN)_2$ analogs lie at much more positive values than those of the O compounds.

Table 4. Analogous reactions of carbonyl compounds and alkylidenemalononitriles.

	Carbonyl compound	Alkylidenemalononitrile	Ref.
Reagent	$>C=O$	$>C=C(CN)_2$	
H_2O	Hydrate formation	Addition of water	[27, 28, 34]
$CN^{\ominus}$	Cyanohydrins	(1-Cyanoalkyl)malononitriles	[28]
$HSO_3^{\ominus}$	Bisulfite adduct	Bisulfite adduct	[28]
PX_3	Zwitterionic adduct	Zwitterionic adduct	[30]
P ylides	Olefination	Olefination (lower yield)	[29]
Dihydropyridines (NADH models)	Alcohols (with NADH-dehydrogenases)	Alkylmalononitriles	[31]
$H_2C<$	Knoevenagel condensation	Adduct formation-elimination only at elevated temperature	[32]
$R_2CHOH/Al(OR)_3$	Meerwein-Ponndorf-Verley reduction	Reduction to alkylmalononitriles (yields lower)	[33]
$NaBH_4$	Alcohols	Alkylmalononitriles	[34]
R—Mg—Hal	Alcohols	Alkylmalononitriles	[39]
	$Cl>C=O$	$Cl>C=C(CN)_2$	
H_2O	Carboxylic acids	Acylmalononitriles	[36, 37]
$N_3^{\ominus}$	Acyl azides	(1-Azidoalkylidene)malononitriles	[37, 38]
Arenes/$AlCl_3$	Friedel-Crafts acylation	Dicyanovinylation	[33—35]
	$RO>C=O$	$RO>C=C(CN)_2$	
R—Mg—Hal	Grignard reaction giving alcohols	Grignard reaction giving monosubstituted malononitriles	[39]
$H_2C(CN)_2$	Aldol reaction	Replacement of RO by $(NC)_2HC$	[40]
	Phenol ester Fries shift	Phenoxymethylene-malononitrile analogous rearrangement (yields lower)	[34]
	$N_3>C=O$	$N_3>C=C(CN)_2$	
Thermolysis	Isocyanate reaction products	Ketenimine reaction products	[41]

4.2. Cyanohydrin Formation

Addition of hydrogen cyanide to aldehydes or ketones affords cyanohydrins. The reactions are known to be strongly accelerated by small amounts of bases. The effective nucleophile appears to be the cyanide ion. Alkylidenemalononitriles react analogously and form anions of (1-cyanoalkyl)malononitriles *(13b)*[28].

$$>C=X + CN^{\ominus} \rightleftharpoons -\underset{CN}{\overset{|}{C}}-X^{\ominus} \quad (13) \qquad (a),\ X = O \qquad (b),\ X = C(CN)_2$$

The (1-cyanoalkyl)malononitriles are strong acids and accordingly form stable salts. This is doubtless the reason why no condensation reaction ensues in the case of alkylidenemalononitriles bearing aromatic substituents. A reaction analogous to the benzoin condensation could not be observed.

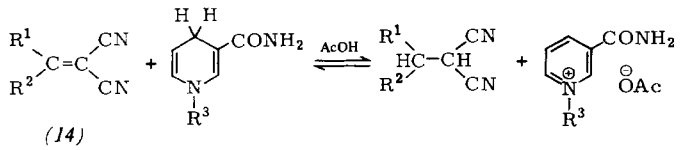
4.3. Reduction

Reduction of aldehydes and ketones usually involves transfer of a proton and of two electrons from the reducing agent to the carbonyl carbon atom. The resulting alkoxide ion is protonated to the alcohol, usually by water. Meerwein-Ponndorf-Verley reduction is formulated as a hydride transfer, and the mechanisms considered are: a cyclic process with participation of one mole of alkoxide per mole of carbonyl compound and a non-cyclic course with participation of two moles of alkoxide per mole of carbonyl compound[42].

We have subjected alkylidenemalononitrile to the conditions of the Meerwein-Ponndorf-Verley reduction[33]; progress of the reaction can easily be monitored with the aid of the amount of acetone formed. The yields of alkylmalononitrile are relatively low however (*p*-nitrobenzylidenemalononitrile gives 15 %, and benzylidenemalononitrile 35 % of the benzyl compound). We suspect that the coordination of the carbonyl oxygen atom with the metal leads to a significantly greater enhancement of positive charge on the adjacent carbon atom than, for example, coordination of the nitrogen atoms in the $C(CN)_2$ compounds. The latter should have relatively little effect on the incorporation of the weakly nucleophilic hydrogen in aluminum isopropoxide. In contrast, complex hydrides with strongly nucleophilic hydrogen, such as sodium tetrahydridoborate, reduce alkylidenemalononitriles in good yields similar to those for aldehydes or ketones[34].

The reduction of carbonyl compounds to alcohols with the aid of dihydropyridines as reducing agent plays a central role in the most varied metabolic pathways of all biological systems. It is essential for the regulation of degradation and synthesis in living cells that these hydrogen transfers are subject to such kinetic hindrance that they can only proceed with the aid of catalyzing proteins (dehydrogenases). It was therefore surprising to find that some alkylidenemalononitriles *(14)* are easily reduced by NADH or model compounds such as 1-benzyl-1,4-dihydronicotinamide without any need for a catalyst, apart from the promotion they may receive from weak acids[31]. Thus the $C(CN)_2$ analogs of certain aldehydes and ketones behave like the quasi-carbonyl compound thiobenzophenone[43] and some carbonyl compounds such as trifluoroacetaldehyde[44] and hexachloroacetone[45] which are highly polarized by halogen substitution. Depending upon the substituents R^1 and R^2 the yields of the reaction lie between 40

and 95%. Remarkably, benzhydrylidenemalonitrile *(14)*, $R^1 = R^2 = C_6H_5$, is not reduced[31], in contrast to the thioanalog of benzophenone.



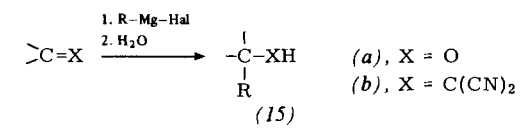
(14)

R^1, R^2 = H, Alkyl, Aryl
R^3 = Benzyl, 2,6-Dichlorobenzyl

The reaction is characterized by a direct transfer of hydrogen from dihydropyridine to the activated olefin, as in biochemical hydrogen transfers and most of the model reactions. Hence no exchange takes place between the dihydropyridine hydrogen and protons of the reaction medium, not even on working in 20% alcoholic acetic acid. This was proved by use of [4,4'-D_2]-1-benzylnicotinamide as reducing agent[31]. The solvent dependence of the isotope effect (H/D = 5—9) is in accord with the concept that transfer of a proton and two electrons takes place in a molecular complex formed from donor and acceptor.

4.4. Reactions with Grignard Compounds

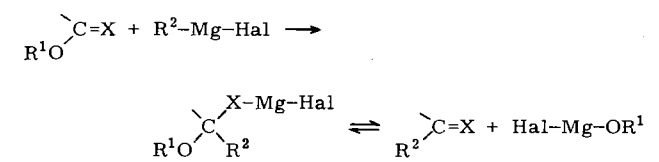
A close similarity exists between the behavior of carbonyl compounds and their $C(CN)_2$ analogs towards Grignard compounds. Thus aldehydes and ketones generally give the alcohols *(15a)* in high yields, and alkylidenemalononitriles the alkylmalononitriles *(15b)*[39].



(15)

(a), X = O
(b), X = $C(CN)_2$

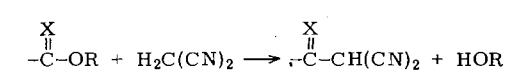
The reaction of Grignard reagents with the $C(CN)_2$ ester analogs has also been investigated[39]. As in the reaction of esters, the labile primary adduct *(16b)* releases an alkoxide ion; reaction to form compounds of type *(15b)* usually follows.



(16)

(a), X = O; *(b)*, X = $C(CN)_2$

This analogous reaction behavior is understandable since Grignard reactions are largely initiated by nucleophilic attack of a potential carbanion on the positively charged carbon atom and the electronegativities of the two structural components therefore play a crucial role in the early phase of the reaction.



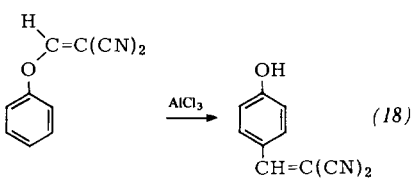
(17)

(a), X = O; *(b)*, X = $C(CN)_2$

Carbonyl compounds and their $C(CN)_2$ analogs also resemble each other in their reactions with CH acids or their carbanions[40, 46]; the reaction leading to *(17a)* or *(17b)* is an appropriate example.

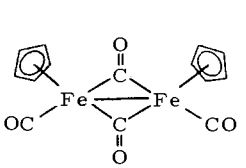
4.5. The Fries Shift

The Fries shift is preferred over direct acylation for the synthesis of aromatic hydroxy ketones. Analogous preparation of aromatic hydroxy aldehydes starting from phenyl formate has been examined by *Olah et al.*[47]. However, instead of rearrangement products they obtained complex condensation products whose formation is rationalized by secondary reactions of the phenol which can arise on acid-catalyzed decarbonylation of both the starting material and the rearrangement product. In spite of this negative result we attempted the analogous reactions[34] starting from *O*-dicyanovinylated phenol, assuming that the elimination of dicyanomethylenecarbene would be less likely, owing to its instability, than the O-analogous decarbonylation. We did indeed obtain a rearrangement product, albeit in only 5% yield, *viz.* *p*-hydroxybenzylidenemalononitrile *(18)*.

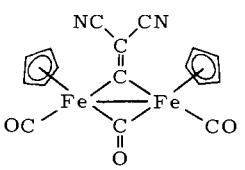


(18)

Free dicyanomethylenecarbene, the $C(CN)_2$ analog of carbon monoxide, has not yet been prepared. The carbene does act as ligand in transition metal complexes such as *(20)*, however, just like carbon monoxide in the complex *(19)*[48, 49].



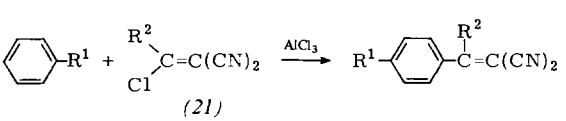
(19)



(20)

4.6. Reactions with Arenes

On proceeding as in the Friedel-Crafts synthesis of ketones, and treating arenes with (1-chloroalkylidene)malononitriles *(21)* in the presence of aluminum chloride, smooth reaction ensues to give the analogous products[35].

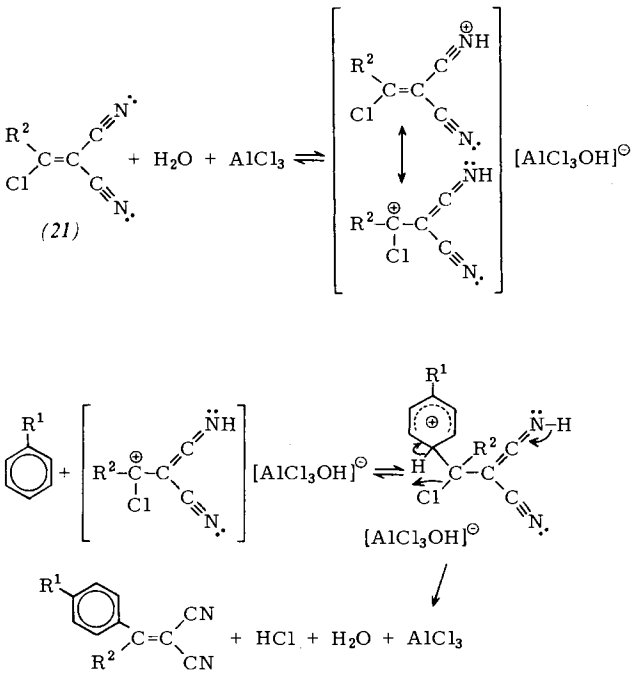


(21)

R^1 = H, CH_3, Cl, OCH_3, OH, also thiophene and naphthalene
R^2 = H, CH_3

We have examined the reaction of numerous arenes with activated olefins, sometimes varying the reaction conditions

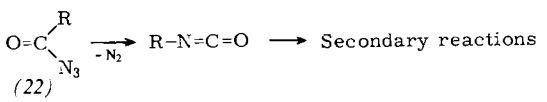
(solvent, temperature, amount of catalyst), and found this reaction to have a wide preparative scope[33-35]. Characteristically, the reaction fails to start in an anhydrous medium. We therefore propose the mechanism depicted in Scheme 3, which is corroborated by spectroscopic evidence[33].



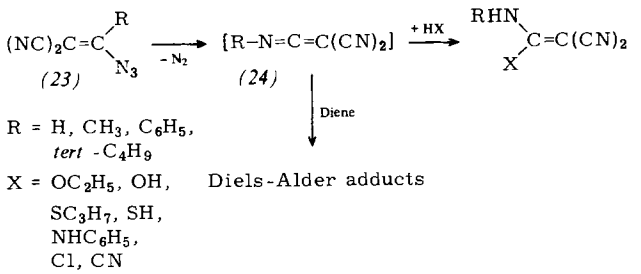
Scheme 3

4.7. Pyrolysis of (1-Azidoalkylidene)malononitriles

By analogy with acyl azides *(22)*, (1-azidoalkylidene)malononitriles *(23)* can be prepared from the corresponding vinyl chlorides[41]. In contrast to most vinyl azides, compounds *(23)* also behave like acyl azides *(22)* on pyrolysis and undergo a Curtius-analogous rearrangement. The ketenimine *(24)* can be detected by trapping reactions.

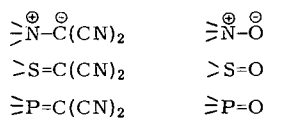


The analogous pyrolysis of the vinyl azides *(23)* is also of broad preparative utility. Its scope is further extended by application to vinyl azides bearing other electron-withdrawing substituents such as COR or COOR in place of the cyano group[36,38,41].



5. Heteroatom Oxides/Heteroatom Dicyano Ylides

The numerous examples of Sections 1 to 4 have shown that the $C(CN)_2$ group, when linked to C or H, imparts the relevant compounds with a close similarity to those of oxygen. This prompted us to consider whether the $C(CN)_2/O$ analogy could also be extended to compounds in which the oxygen is bonded to the heteroatoms N, S, or P (Scheme 4).

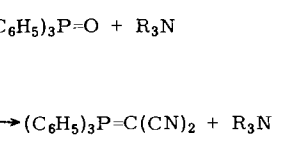


Scheme 4

Although dicyano ylides have been known for several years, until recently the only reports about them in the literature were of a physico-chemical nature; these include dipole moments, X-ray structural data, and spectroscopic data. The reason was probably that the dicyano ylides are far more stable than other ylides and there was therefore little incentive to subject them to the usual ylide reactions[50]. In their reactions they resemble oxides more closely than other ylides, as is immediately apparent from their stability.

5.1. Amine Oxides and Nitrogen Dicyano Ylides

On comparison of the reactions of nitrogen dicyano ylides *(26)* with those of the amine oxides *(25)* it is instructive to consider the reaction with triphenylphosphane.



(25)

(26)

Aliphatic amine oxides transfer their oxygen almost quantitatively to triphenylphosphane in boiling glacial acetic acid[53]. In contrast, aromatic amine oxides prove to be very inert towards triphenylphosphane; they only react above 200 °C and then in low yields[54]. The $C(CN)_2$ group is transferred analogously from nitrogen dicyano ylides to triphenylphosphane. We have investigated this transylidation with six different nitrogen dicyano ylides[51,52]; they were all less reactive than the oxides. An analogy is noted, however, in the gradation of reactivity. For instance, trimethylammoniodicyanomethanide *(26)*, R = CH_3, reacts at lower temperature (160 °C) and faster (16 h), giving far better yields (60 %) of triphenylphosphoniodicyanomethanide than pyridiniodicyanomethanide (210 °C/24 h/8.5 %).

5.2. Sulfoxides and Sulfur Dicyano Ylides

Numerous reports about physico-chemical studies on the structure of sulfoxides and sulfur dicyano ylides are encountered in the literature. Together with our findings the following picture can be drawn[51]:

1) Sulfoxides and sulfur dicyano ylides are not planar but pyramidal molecules, whose apices are occupied by two C

atoms, the S atom, and the O atom or the $C(CN)_2$ group (X-ray structure analysis, NMR spectra).

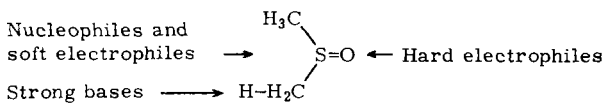
2) The S atom in sulfoxides and sulfur dicyano ylides is sp^3 hybridized; there is a polar $d\pi$—$p\pi$ bond between S and O or between S and $C(CN)_2$ (X-ray structure analysis, dipole moment, basicity).

3) Both in sulfoxides and in sulfur dicyano ylides interaction exists between the sulfur lone pair and the π-electron systems of unsaturated substituents (X-ray structure analysis, UV spectra).

4) Sulfoxides and sulfur dicyano ylides are only weakly basic. The pK_{BH^+} lie between those of the phosphane oxides (around -2) and that of acetone (-7.0).

5) X-Ray structure analysis and IR spectra indicate interactions between the carbanion electron pair and the CN groups in sulfur dicyano ylides.

A suitable reference substance for chemical reactions was dimethyl sulfoxide (DMSO) whose properties as solvent and reactant have attracted so much attention that there is nowadays hardly any other organic compound so thoroughly studied and for which such a broad range of applications has been discovered. Scheme 5 shows the reactive sites of the DMSO molecule[55].

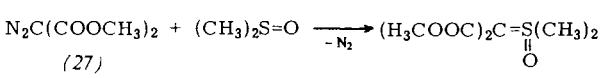


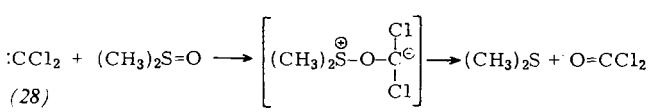
Scheme 5

We have carried out detailed comparisons of thermal decomposition, basicity and salt formation, as well as the reactions with diazomalononitrile, sodium hydride/benzyl chloride, chlorinating agents, acyl chlorides, methyl iodide, and triphenylphosphane with the corresponding reactions of the ylides.

5.2.1. Reaction with Diazomalononitrile

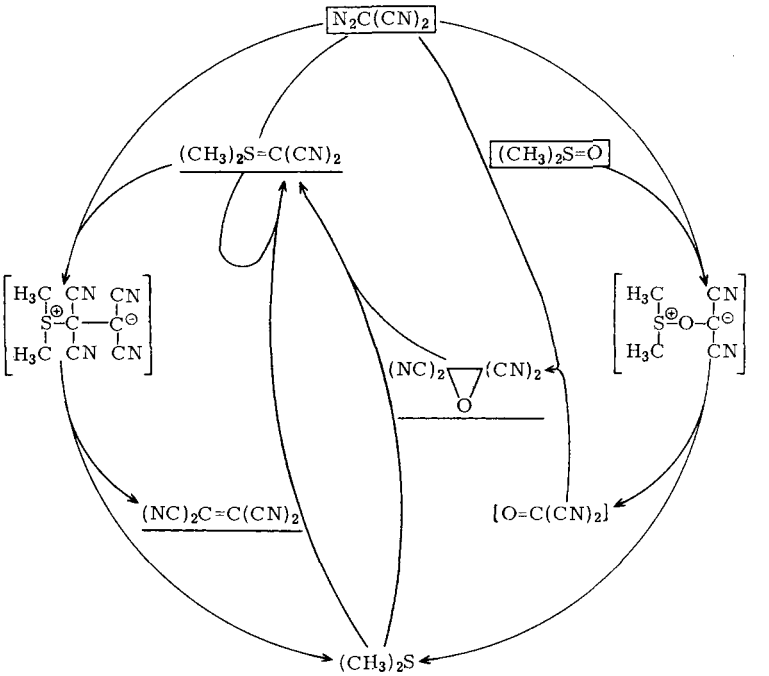
Sextet intermediates of carbene type are trapped by DMSO to form sulfoxonium ylides, *e.g.* in the reaction with dimethyl diazomalonate *(27)*[56], or oxidized, *e.g.* dichlorocarbene *(28)* to phosgene[57].





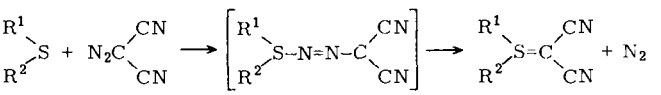
The reaction of DMSO with diazomalononitrile leads to dimethylsulfoniodicyanomethanide, dimethyl sulfide, tetracyanoethylene, and tetracyanoethylene oxide (and nitrogen). This finding supports the reaction course shown in Scheme 6[58].

The secondary reaction of the sulfide with diazomalononitrile shown in Scheme 6 is frequently the method of choice for preparing sulfur dicyano ylides *(29)*, particularly those bearing aryl substituents[51, 58].

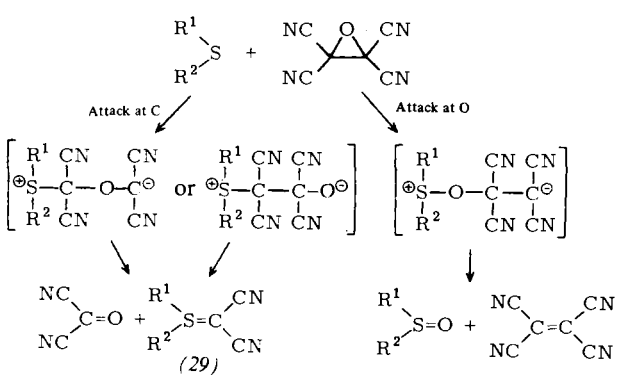


Scheme 6. Starting materials are shown in boxes, intermediates enclosed in brackets, and isolated products underlined.

Tetracyanoethylene is obtained as by-product (as in Scheme 6). This compound and sulfide were invariably isolated when we carried out the direct reaction of sulfur dicyano ylides with diazomalononitrile[51, 58]. The reaction of the sulfide with



tetracyanoethylene oxide can likewise be utilized for the preparation of sulfur dicyano ylides[51, 59, 60]. Sulfides containing bulky aryl or aralkyl substituents also attack the oxygen; the product ylide *(29)* is then accompanied by the sulfoxide (Scheme 7)[51, 59].



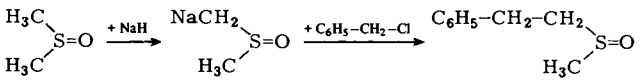
Scheme 7

Thus in this reaction both the oxygen and the $C(CN)_2$ group of tetracyanoethylene oxide are transferred to a sulfur atom.

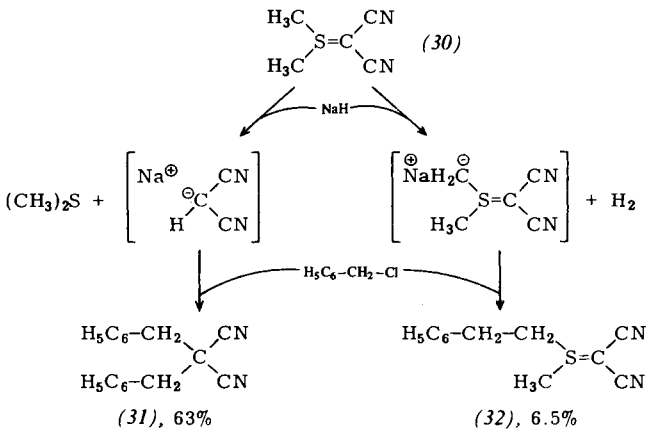
5.2.2. Reaction with Sodium Hydride and Benzyl Chloride

One of the best known reactions of dimethyl sulfoxide is deprotonation by strong bases, leading to the methylsulfinyl

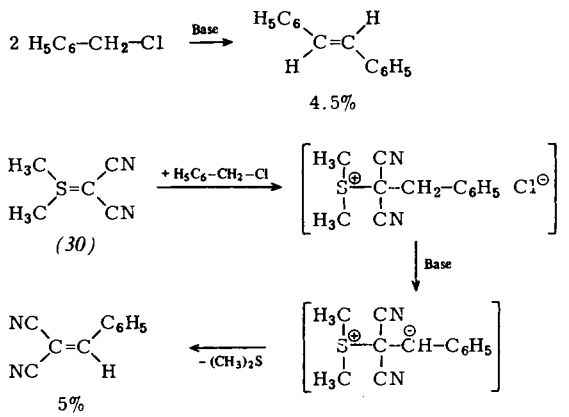
carbanion which can undergo numerous further reactions. For purposes of comparison we chose benzylation after prior treatment with sodium hydride[61].



Reaction with dimethylsulfoniodicyanomethanide *(30)* gives only low yields of the analogous reaction product, *viz.* methylphenethylsulfoniodicyanomethanide *(32)*. The principal reaction is cleavage of the ylide bond with subsequent benzylation giving dibenzylmalononitrile *(31)*.

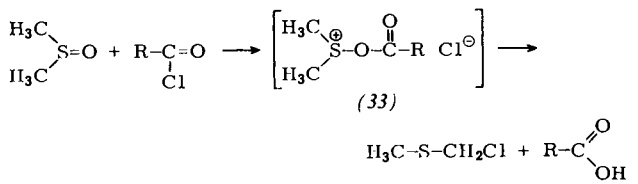


Further products obtained are *trans*-stilbene, which also occurs as by-product of reaction with DMSO[61], and benzylidenemalononitrile, which is probably formed by analogy with the Kornblum aldehyde synthesis with DMSO[62].

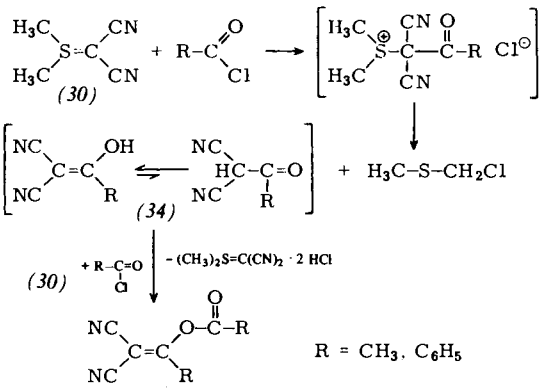


5.2.3. Reaction with Acyl Chlorides

DMSO reacts with acyl chlorides *via* the acyloxysulfonium salts *(33)* as intermediates to give carboxylic acids and chloromethyl methyl sulfide[63,64].

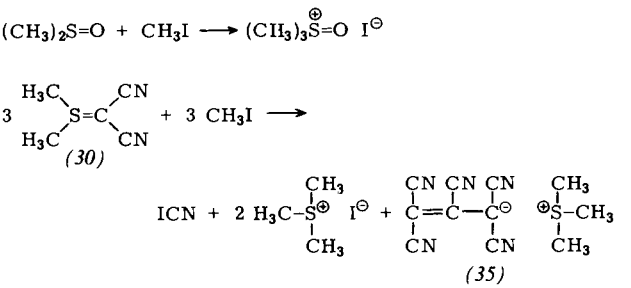


We assume that the primary step of the reaction of the ylide *(30)*[51,58] is acylation of the cyano-substituted carbon atom, as in the reaction with DMSO. The acylation product then decomposes to chloromethyl methyl sulfide and acylmalononitrile *(34)*. The latter, which preferably exists as the enol, is once again acylated as such, with the ylide *(30)* acting as a base. Support for this reaction comes from formation of the same product on acylation of the corresponding potassium enolates.

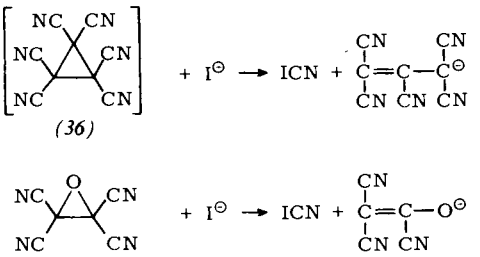


5.2.4. Reaction with Methyl Iodide

Reaction with methyl iodide leads to trimethylsulfoxonium iodide in the case of DMSO[65], and to trimethylsulfonium iodide, cyanogen iodide, and trimethylsulfonium pentacyanopropenide *(35)* in the case of dimethylsulfoniodicyanomethanide *(30)*[51,58].



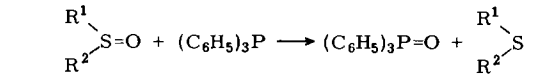
The initial product is most likely a salt analogous to that formed in the DMSO reaction, whose decomposition affords trimethylsulfonium iodide and unites three $C(CN)_2$ fragments. Hexacyanocyclopropane *(36)* is a conceivable intermediate which would doubtless react immediately with iodide ions to give pentacyanopropenide and cyanogen iodide; the analogous reaction of tetracyanoethylene oxide is known[66].

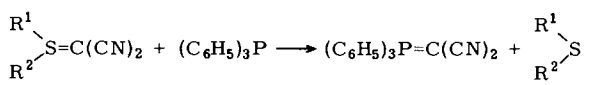


5.2.5. Reactions with Triphenylphosphane

The reaction of sulfoxides with phosphanes involves transfer of oxygen from sulfur to phosphorus. The mechanism of the

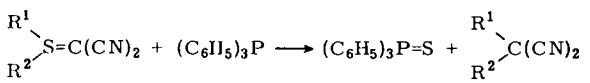
actual oxygen-transfer step is strongly dependent on the nature of the substituents attached to the two heteroatoms and on the reaction conditions such as temperature, catalyst, and solvent[67–69]. Most investigations employed the least reactive phosphane, triphenylphosphane; triphenylphosphane oxide and the relevant sulfide are obtained.



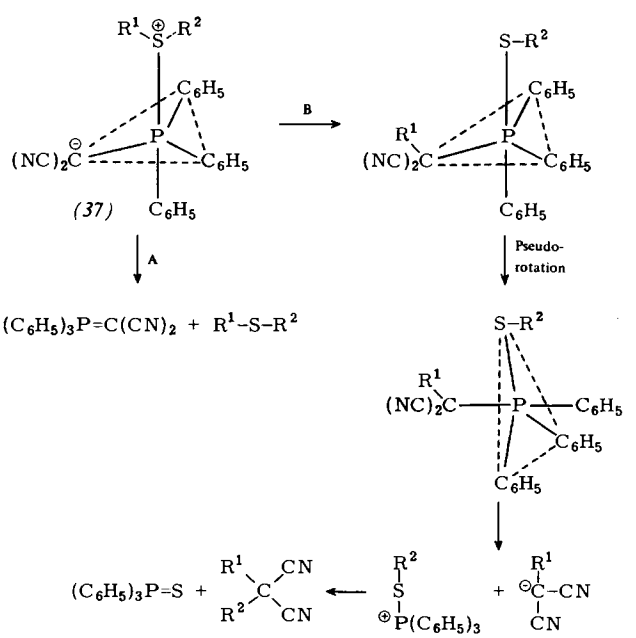


We have treated a series of sulfur dicyano ylides carrying various substituents on the sulfur with triphenylphosphane in the melt and in all cases observed the analogous $C(CN)_2$-transfer reaction giving the phosphorus dicyano ylide[51, 70].

Thus transylidation is the sole or predominant reaction on use of sulfur dicyano ylides bearing aromatic substituents on the sulfur. With dialkyl- and diaralkylsulfoniodicyanomethanides, however, it occurs only as a side reaction; the major reaction is then transalkylation, in which the substituents migrate from sulfur to the dicyano-substituted carbon atom while the sulfur is taken over by the phosphorus to form triphenylphosphane sulfide[71].



In order to interpret the reactions (Scheme 8)[70], we assume that the initial step is addition of triphenylphosphane to the ylide bond giving adducts *(37)* with five ligands on the phosphorus atom. Elimination of the sulfide from the apical position then gives the transylidation products by route A. The alkyl shift from the apical sulfonium sulfur to the equatorial carbanion center according to path B modifies the electronega-



Scheme 8

tivity gradation of the ligands. This leads to a rearrangement of the pseudorotation type[72]. Rupture of the P—C bond, which is now the weakest linkage, leads after subsequent alkylation of the fragments as a secondary reaction to the transalkylation products.

6. Conclusion

Strict classification of organic reactions according to the elemental composition of the compounds, to the type of bonding, and to the functional groups present is unable to cater for a large number of "anomalous" reactions. There are poorly defined boundaries between O—H and C—H acids, between carbonyl compounds and olefins, between heteroatom oxides and ylides. Comparisons of reactivity as described above serve to help us understand the finer points of the way in which "normal" and "anomalous" reactions proceed. Moreover, our thinking within the framework of this analogy permitted the discovery and interpretation of several novel reactions. The utility of this conceptual approach largely depends upon our remembering that no comparison is perfect.

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New synthetic methods (15)

The Synthetic Utility of 2-Oxazolines[**]

By A. I. Meyers and E. D. Mihelich[*]

The oxazoline ring system, first prepared in 1884, has only in the last five years been shown to possess considerable utility in the synthesis of a variety of functionalized organic compounds. By appropriate metalation of the 2-alkyl substituent it is possible to prepare a variety of homologated carboxylic acid derivatives, both chiral and achiral. Various other manipulations of the oxazoline ring lead to aldehydes, ketones, lactones, amino acids, thiiranes, and olefins. Due to the inertness of the oxazoline ring system to various reagents (RMgX, $LiAlH_4$, CrO_3, mild acid or alkali) it may be utilized as a protecting group for carboxylic acids during the transformations involving the above reagents. Two major new developments in oxazoline chemistry involve a) the use of a chiral oxazoline as a reagent for asymmetric syntheses of chiral carboxylic acids, lactones, alcohols, thiiranes, and olefins and b) a new mode of aromatic substitution in which the aryloxazolines act as nucleophilic or electrophilic reagents. This behavior has led to a variety of polysubstituted benzenes and biphenyls which would be inaccessible by classical routes. A variety of examples illustrating the utility of oxazolines indicated above are presented so that the reader may appreciate the vast potential of this simple ring system in synthesis.

1. Introduction

As organic chemists attempt syntheses of increasingly complex molecules, the need for efficient, mild, and selective functional group transformation and elaboration becomes ever more apparent. The ability of a heterocycle to meet these requirements is not a new idea[1]. In general, however, this concept has not been generally accepted for synthesis. The introduction and rapid acceptance of dithianes[2], oxazines[3], isoxazoles[4], and other heterocycles as versatile tools of the synthetic chemist result predominantly from their ability to 1) remain inert to a variety of commonly used reagents, 2) perform a desired transformation efficiently and under mild conditions, and 3) be available for further modification *via*

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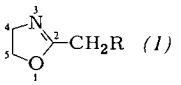
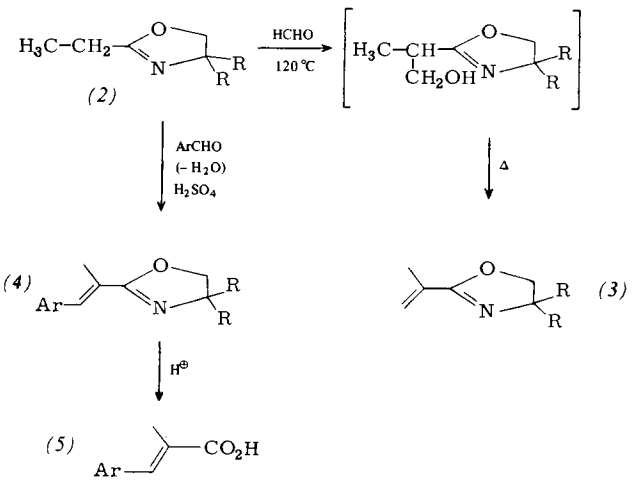
[**] Abbreviations: Me = methyl, Et = ethyl, Pr = propyl, Bu = butyl, Pent = pentyl, Hex = hexyl, Ar = aryl, Ph = phenyl, Tos = *p*-toluenesulfonyl, LDA = lithium diisopropylamide, DME = dimethoxyethane, HMPA = hexamethylphosphoric triamide.

mild or neutral "releasing" conditions. These properties, commonly identified with "latent functionality"[5], provide a flexibility which is both rare and extremely valuable to the chemist involved in synthesis.

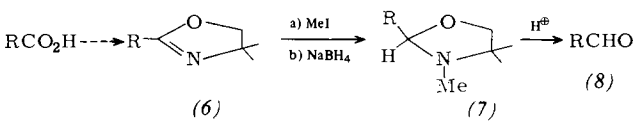


(1)

2-Substituted 2-oxazolines *(1)*, although well-known compounds[6], are newcomers to this elite group of molecules. Earlier reviews[6] emphasized the industrial importance of monomeric and polymeric 2-oxazolines since few uses in synthesis had been reported. The 2-substituted 2-oxazoline ring was recognized, however, as having a number of potentially useful properties. The α-hydrogen in *(1)* was shown to be labile and to undergo aldol-type condensation with formaldehyde[6a] and aromatic aldehydes[7] leading to oxazolines *(3)* and *(4)*, respectively, bearing an unsaturated side chain. Compounds *(4)* are hydrolyzed in aqueous acid to unsaturated carboxylic acids *(5)*. *Nordin*[8] found that carboxylic acids may be transformed into aldehydes *(8)* *via* the oxazoline *(6)* if it is first methylated and then reduced with sodium tetrahydridoborate to *(7)*.



Research in oxazoline chemistry has been greatly aided by their ready availability. The classical methods[9,10] utilizing α-amino alcohols and carboxylic acids provide ready access to 2-alkyl- and 2-aryloxazolines. More recent preparations

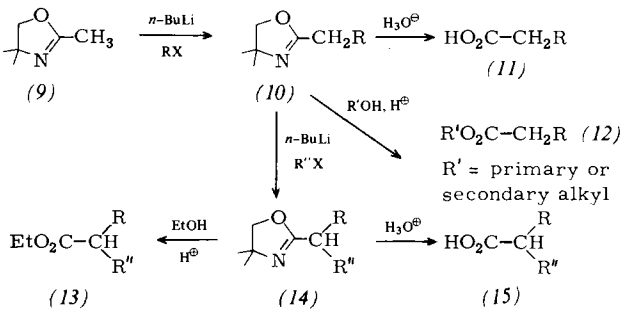


(6) *(7)* *(8)*

involve the condensation of α-amino alcohols with isocyanides[11], nitriles[12], cyanoallenes[13], and propargylphosphonium salts[14]. These preparations foreshadowed the explosion in oxazoline research over the past five years which has led to a multitude of functionally diverse products through suitable manipulations of the oxazoline nucleus. A summary of this work by product type is presented below.

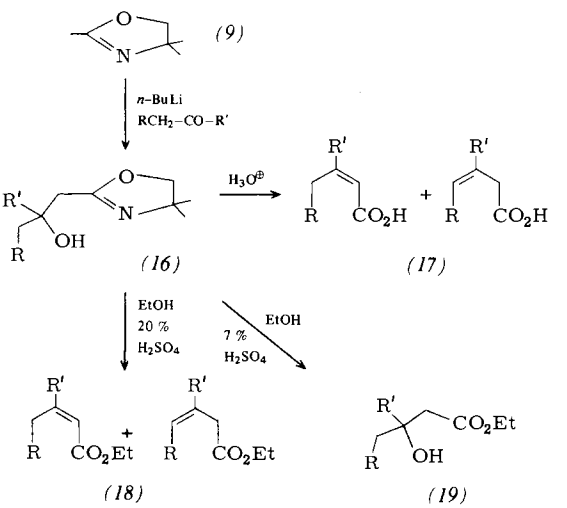
2. Aliphatic Carboxylic Acids and Esters

The simple oxazoline *(9)*[15] may be metalated with a variety of lithio bases [butyllithium, phenyllithium, lithium diisopropylamide (LDA), and lithium bis(trimethylsilylamide) at −78 °C and treated with alkyl iodides or bromides to afford the elaborated oxazoline *(10)* in excellent yields (93—99 %). Acidic hydrolysis affords the homologated acetic acid *(11)*, whereas alcoholysis provides the homologated esters *(12)* in yields of 77—98 %. Dialkylations (but not trialkylations) are also feasible by metalation of the 2-alkyloxazoline *(10)* followed by addition of a second equivalent of alkyl halide furnishing the 2-(dialkylmethyl)oxazolines *(14)*. Hydrolysis or alcoholysis once again leads to the dialkyl acetic acids *(15)* or the corresponding esters *(13)*. In this fashion, a number of carboxylic acid derivatives were prepared in good yield[16].



(9) *(10)* *(11)* *(12)* *(13)* *(14)* *(15)*

Unsaturated acids or esters were also prepared *via* this technique by utilization of carbonyl compounds. Thus, the 2-methyloxazoline *(9)*, when metalated and treated with various carbonyl compounds, gave high yields of the hydroxy derivative *(16)* which may be cleaved in aqueous acid to a "thermodynamic" mixture of α,β- and β,γ-unsaturated acids *(17)*. Alternatively, use of 20% H_2SO_4/ethanol provided good yields of the unsaturated esters *(18)*. Of further interest was the fact that cleavage of the oxazoline ring in *(16)* could be readily accomplished without loss of the β-hydroxy group by heating in 7% H_2SO_4/ethanol. In this way, good (80—87 %) yields of β-hydroxy esters *(19)* were obtained. This last result should be a useful alternative to the Reformatsky reaction and more recent routes to this class of compounds[17].



(9) *(16)* *(17)* *(18)* *(19)*

2.1. Optically Active Carboxylic Acids

An efficient asymmetric synthesis of 2-alkyl carboxylic acids *(24)* in 51—86% enantiomeric excess (ee) was recently developed based upon the synthetic properties of 2-alkyloxazo-

lines[18]. The readily available (+)-amino diol *(20)*[19] was transformed into the chiral 2-alkyloxazoline *(21)*[19b,c] which was metalated, using lithium diisopropylamide, to the lithio derivative *(22)*. Alkylation with a wide variety of alkyl halides gave *(23)* which was then hydrolyzed in 4 N sulfuric acid to either the (*R*) or (*S*) carboxylic acid *(24)*. The method, in addition to high optical yields, allows one to *predictably prepare either enantiomer* by proper introduction of R and R′ (Table 1). The methoxyamino alcohol *(25)* was also efficiently recovered and could be reused to prepare the starting oxazoline *(21)*.

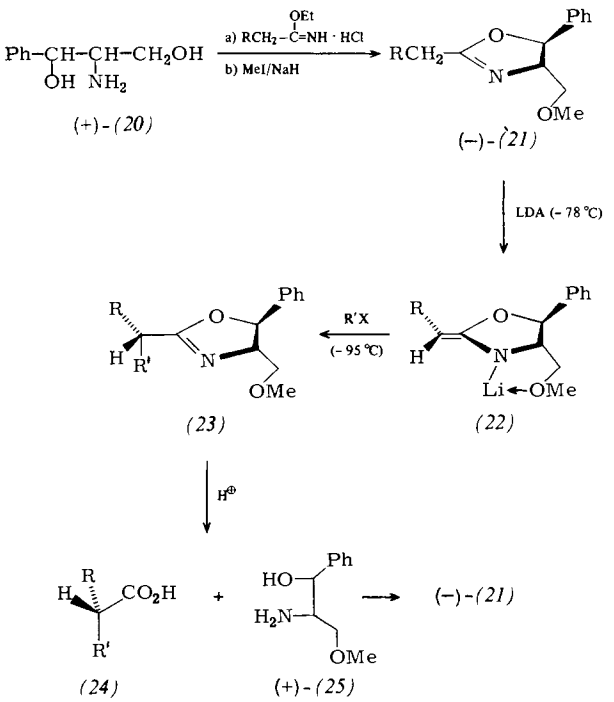
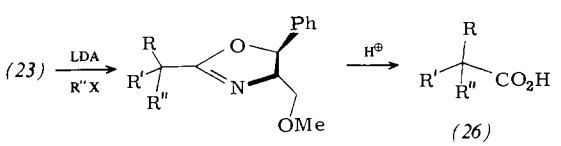


Table 1. Optically active 2-alkyl carboxylic acids *(24)* from chiral oxazolines *(21)*. Alkyl halides or sulfates were added at −98 °C.

R	R'X	Overall yield [%]	ee [%] [a]	Configuration
Me	EtI	84	78	*S*
Et	Me_2SO_4	83	79	*R*
Me	*n*-PrI	79	72	*S*
n-Pr	Me_2SO_4	74	72	*R*
Me	*n*-BuI	65	75	*S*
n-Bu	Me_2SO_4	78	70	*R*
Me	$PhCH_2Cl$	62	74	*S*
$PhCH_2$	Me_2SO_4	75	78	*R*
Et	$PhCH_2Cl$	30	85	*S*
$PhCH_2$	EtI	37	73	*R*
n-Bu	$PhCH_2Cl$	41	82	*S*
$PhCH_2$	*n*-BuI	35	86	*R*
Ph	EtI	42	51 [b]	*R*
Ph	*n*-PrI	57	56 [b]	*R*
Ph	*i*-PrI	22	65 [b]	*R*

[a] ee = enantiomeric excess.
[b] Accompanied by 8—10 % racemization due to increased acidity of benzyl protons.

An attempt to prepare chiral trialkylacetic acid from *(23)* gave trialkylacetic acids *(26)*, but the products were nearly



racemic[20]. It is important to note that 2-trialkylmethylated oxazolines could not be prepared from simple oxazolines *(9)*. The presence of the methoxyl group in the chiral oxazolines serves to stabilize the lithio derivative *(22)* and presumably allows metalation to occur.

2.2. Kinetic Resolutions

The chiral oxazoline *(27)*, when transformed into its lithio derivative *(28)*, was capable of chiral recognition with respect to racemic alkyl iodides[21]. In a variety of examples, the (*S*)-enantiomer of 2- and 3-iodoalkanes was alkylated faster by *(28)* leaving the (*R*)-enriched halide enantiomer to be recovered (30—49% ee). The (*R*)-enriched 3-alkyl carboxylic acid *(31)* was also recovered (30—47 % ee) after hydrolysis of the alkyloxazoline *(30)*. In most cases the enantiomeric excess for halide and acid differed by less than 8 % (Table 2). This method therefore allows a) establishment of absolute configuration of alkyl halides and 3-alkyl carboxylic acids without the need for any optically active materials except *(27)*, b) prediction of the maximum rotation of either alkyl halide or acid as long as one of them is reliably known,

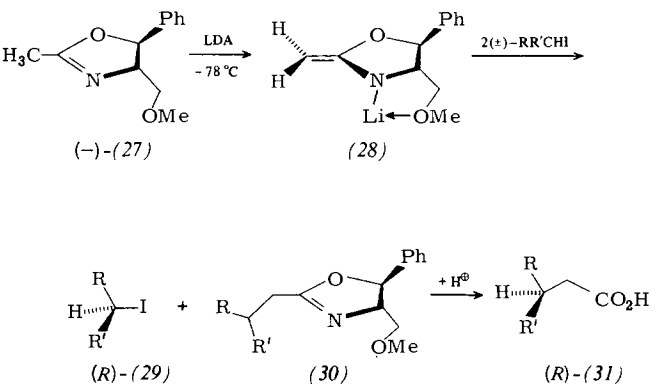


Table 2. Kinetic resolution of alkyl iodides and synthesis of the optically active 3-alkyl carboxylic acids *(31)*. The alkyl iodides were added to *(28)* between −50 and −70 °C; the reaction time was 8 to 30 h. The values given in parentheses are our own; the optically active compounds were hitherto unknown.

		Alkyl iodide recovered			Acids *(31)*		
R	R'	Yield [%]	ee [%] [a]	Config.	Overall yield [%]	ee [%] [a]	Config.
Me	Et	41	34	*R*	86	34	*R*
Me	Pr	60	31	*R*	89	39	*R*
Me	Bu	43	49	*R*	85	47	*R*
Me	Hex	83	31	*R*	81	39	*R*
Et	Pr	50	(31)	*R*	71	31	*R*
Et	Bu	125 [d]	46 [b]	*R*	48	20 [b]	(*R*)
Et	Pent	120 [d]	(58)	*R* [c]	54	(58)	*R*

[a] ee = enantiomeric excess.
[b] Both halide and acid were known but the large variance in optical purity suggests that one or both $[\alpha]_D$ values for the pure compounds are incorrect.
[c] Configuration assigned based on the configuration of the acid.
[d] Yield defined here as amount of halide recovered in excess of 50%.

c) confirmation of the rotation of pure enantiomers as long as one is reliably known. Thus, failure to achieve comparable percentage enantiomeric excesses for halide or acid clearly indicates that the reported values are unreliable.

2.3. Optically Active 3-Alkyl Carboxylic Acids

Chiral 2-(1-alkenyl)oxazolines *(32)* undergo 1,4-addition with organolithium reagents at −78 °C to form the adduct *(33)* which, after hydrolysis (3—6 N H_2SO_4, reflux, 3—6 h), leads to the 3-alkyl carboxylic acids *(34)* in exceedingly high optical yields (Table 3).

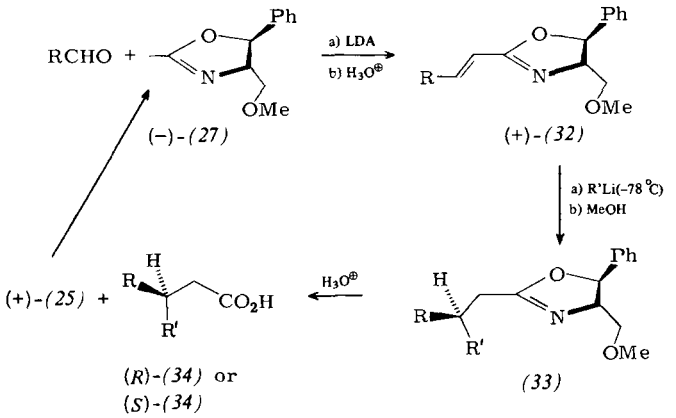


Table 3. Optically active 3-alkylalkanoic acids *(34)*.

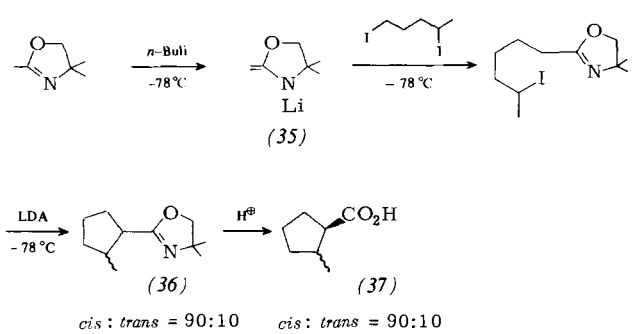
R	R' [a]	Overall yield [%]	ee [%] [b]	Config.
Me	Et	30	92	*R*
Me	*n*-Bu	38	91	*R*
Me	Ph	34	98	*S*
Et	*n*-Bu	49	(61) [c]	*R*
Et	Ph	31	92	*S*
Ph	Et	66	97	*R*
c-Hexyl	Et	75	99	*R*
c-Hexyl	*n*-Bu	76	99	*R*

[a] To date, methyllithium has not been added to (+)-*(32)*. [b] ee = enantiomeric excess. [c] The literature value is questionable and thus this may not reflect the true enantiomeric purity.

Once again, either enantiomer may be formed by appropriate choice of the R and R'[22]. The chemical yield for this process is sometimes low and this is due mainly to competing allylic proton abstraction from *(32)*. However, when R is phenyl or contains only a tertiary proton, this side reaction becomes less serious.

2.4. Cyclic Carboxylic Acids

A stereoselective synthesis of *cis*-2-methylcyclopentanecarboxylic acid *cis-(37)* was achieved by successive treatment of the lithiooxazoline *(35)* with 1,4-diiodopentane furnishing a 90:10 mixture of the oxazolines *(36)* (NMR and VPC).



Hydrolysis gave *(37)* as the major product[23] (70 % overall yield). Note that this reaction leads to the thermodynamically less stable isomer.

3. Butyrolactones

The reaction of lithiooxazolines *(35)* with a variety of epoxides *(38)* results in nucleophilic ring opening to the adducts *(39)* in good yield. Hydrolysis in aqueous acid furnished the butyrolactones *(40)* in overall yields of up to 76% (Table

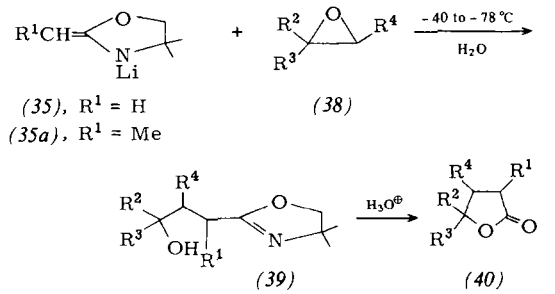
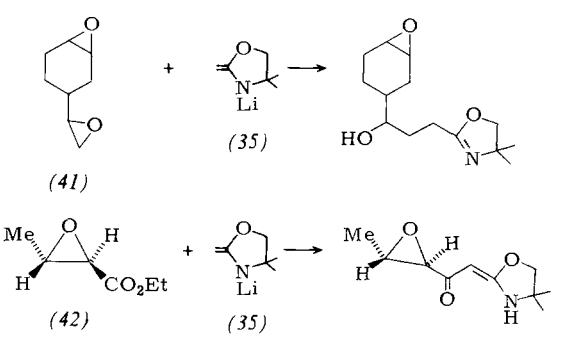


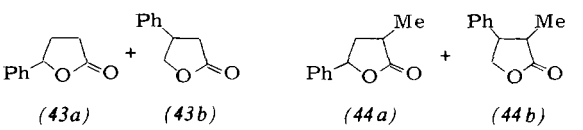
Table 4. Butyrolactones *(40)* from 2-oxazolines.

R^1	R^2	R^3	R^4	Overall yield [%]
n-Pent	H	H	H	72
n-Pent	H	Et	H	76
H	Me	Me	H	72
H	*n*-Hex	Me	H	70
H	—$(CH_2)_5$—		H	56
$PhCH_2$	Me	Me	H	70
H	H	—$(CH_2)_4$—		65
H	H	Me	*n*-Pent	≈0
H	H	Me	Me	16

4)[24]. The efficiency of the epoxide ring opening was sensitive to substituents present, and it was observed that 1,2-disubstituted epoxides containing bulky group reacted poorly if at all under the conditions employed. Thus, cyclooctene oxide failed to react whereas compounds containing two epoxy functions could be selectively alkylated [*e.g. (41)* and *(42)*].

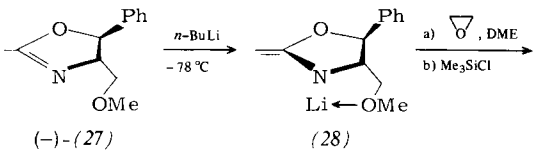


Styrene oxide gives a mixture (94:6) of two isomeric lactones *(43a)* and *(43b)* whereas the lithio-α-methyloxazoline *(35a)* gives a 60:40 mixture with styrene oxide [*(44a)* and *(44b)*]. (For reactions of other lithiated heterocycles with styrene oxide see ref. [25].)

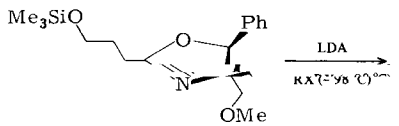


3.1. Optically Active Butyrolactones

The use of a chiral oxazoline *(27)* for the asymmetric synthesis of chiral α-alkylbutyrolactones *(47)* was also demonstrated and gave the latter in 65—75 % enantiomeric excess[26] (Table 5). This can be regarded as a routine extension of the asymmetric synthesis of 2-alkyl carboxylic acids (see Section 2). Alternatively, the optical antipode of *(47)* can be prepared by reversal of the introduction of electrophiles. Since ethylene oxide reacts too slowly at −78 °C, it is necessary to use an equivalent unit and 2-iodoethyloxytrimethylsilane *(48)* was employed. Alkylation of the chiral lithiooxazoline



(−)-(27) *(28)*



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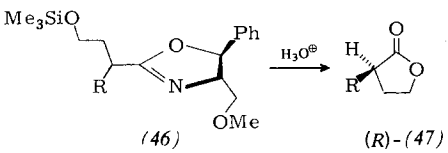


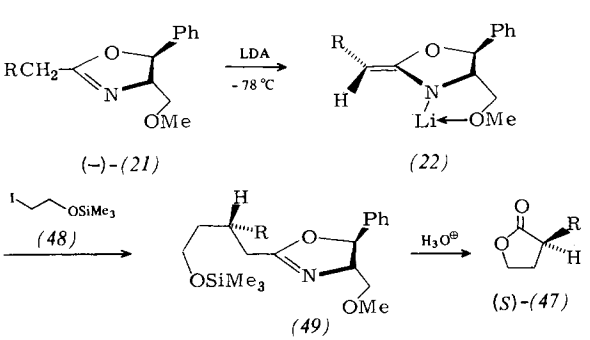
(46) *(R)-(47)*

Table 5. Optically active (*R*)-2-alkylbutyrolactones *(47)*.

RX	Overall yield [%]	$[\alpha]_D^{23}$ (*c* EtOH) [a]	ee [%] [b]	$CD_{(CH_3CN)}$ $[\Theta]_{218\,nm}$
Me_2SO_4	58	+14.80 (10.0)	69	−1430
EtI	68	− 7.65 (9.8)	[c]	−1750
n-PrI	75	− 8.05 (5.7)	73	−1870
Allyl-Cl	60	−16.50 (4.8)	72	−1730
n-BuI	71	− 7.30 (9.7)	[c]	−1600

[a] Concentration *c* in g/100 ml.
[b] ee = enantiomeric excess.
[c] Not reported in the literature. However, based on the CD spectrum it may be assumed to be between 60—70 % enantiomeric excess.

(22) gave the adduct *(49)*, which hydrolyzed to the (*S*)-lactone *(47)* in comparable optical purity[27] [R = allyl, $[\alpha]_D = +20.0°$, ee = 86 %; R = *n*-butyl, $[\alpha]_D = +8.7°$, ee = 70—80 %].

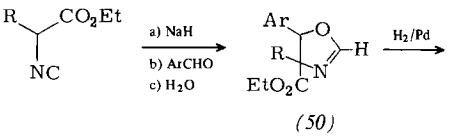


(−)-(21) *(22)*

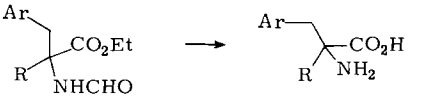
(48) *(49)* *(S)-(47)*

4. Amino Acids

Schöllkopf[28] has demonstrated the use of oxazolines *(50)* in an efficient synthesis of α-amino acids *(52)*. The yields



(50)

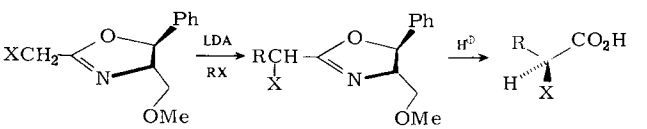


(51) *(52)*

of the *N*-formyl precursor *(51)* were very high (95—99 %) in this sequence.

5. Optically Active 2-Chloro and 2-Methoxy Carboxylic Acids

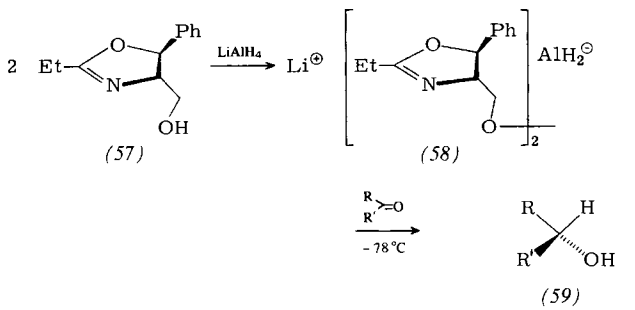
Chiral oxazolines *(53)* and *(54)* have been employed to prepare optically active 2-chloro acids *(55)* and 2-methoxy acids *(56)* in 50—65 % overall yield[29]. The percentage enantiomeric excesses for these products were not unusually high and further work is required. This method may also have potential for an efficient synthesis of these classes of compounds using achiral oxazolines.



(−)-(53), X = Cl R = Me, Et, Pr, Bu *(S)-(55)*, X = Cl
(−)-(54), X = MeO *(R)-(56)*, X = MeO

6. Optically Active Alcohols

The unusual stability of 2-oxazolines toward Grignard compounds and lithium tetrahydridoaluminate[48] was also put to use in a study of asymmetric additions to prochiral carbonyl compounds[30]. Treatment of *(−)-(57)* with 0.45 equiv. of $LiAlH_4$ gave an alkoxide *(58)* of undetermined structure and when treated with a variety of prochiral carbonyl compounds (−78 °C, THF) gave chiral alcohols of 4—65 % ee (Table 6). The chiral oxazoline was recovered for further use in 88—91 % yield. As seen from Table 6, aryl ketones gave reasonable degrees of asymmetric reduction (except α-tetralone) whereas alkyl ketones produced the corresponding alcohols in poor enantiomeric excess. Although these results, using a chiral oxazoline, are still far from perfect, they indicate that *(57)* mediates asymmetric reduction of ketones as well as a variety of other chiral systems (Table 7). To date, the asymmetric



(57) *(58)* *(59)*

reduction of ketones to chiral alcohols in an efficient and general manner still eludes synthetic methodology.

Table 6. Asymmetric reductions of ketones with $LiAlH_4 \cdot 2$ *(57)* at −78 °C in tetrahydrofuran.

Ketone	Alcohol	Yield [%]	$[\alpha]_D^{25}$ [a]	ee [%][b]	Config.
MeCOPh	MeCH(OH)Ph	80	+28.4	65	*R*
EtCOPh	EtCH(OH)Ph	81	+17.2	62	*R*
i-PrCOPh	*i*-PrCH(OH)Ph	78	+20.4	43	*R*
α-Tetralone	α-Tetralol	89	+ 1.21	3.7	*S*
2-Octanone	2-Octanol	80	− 0.55	6	*R*

[a] Neat.
[b] ee = enantiomeric excess.

reagent [to give *(62)*] and treated with various carbonyl compounds at different temperatures. The resulting alcohols *(64)* were obtained in good yield (80—90 %) but in only low enantiomeric excess (0.5—17 %). On the other hand, the methyloxazolinol *(61)* was treated with 1.7 equiv. of RMgBr [to form *(63)*] and added to carbonyl compounds under various conditions. Once again, the addition proceeded in 80—95 % yield but the optical efficiency of the reactions was only 9—25 % ee (Table 8). It is interesting to note, however, that the Grignard reaction using *(60)* gave 1-phenylethanol of opposite configuration to that utilizing *(61)*. Once again the asymmetric induction is somewhat disappointing but compares favorably with other reported attempts to prepare chiral alcohols from Grignard complexes[37, 38].

Table 7. Comparison of various asymmetric reducing agents. Optical purities [%] and configurations of secondary alcohols.

Ketone	$LiAlH_4$/ Alkaloid [31]	$LiAlH_4$/ Monosaccharide [32]	AlH_3/ Amine [33]	R$_3$Al [34]	$LiAlH_4$/ Darvon [35]	$LiAlH_4$/ *(57)* [c]
MeCOPh	48 *R*	71 *R*	84 *S* [a]	6 *S*	68 *R*	65 *R*
EtCOPh	—	46 *R*	—	13 *S*	—	62 *R*
i-PrCOPh	—	—	—	44 *S* [b]	30 *R*	43 *R*
α-Tetralone	—	—	—	0	—	3.7 *S*
$MeCOCH_2Ph$	3 *R*	—	16 *S* [a]	—	—	0.5 *S*
2-Octanone	6 *S*	25 *R*	—	—	—	4 *S*

[a] Reduction yield 50 %. [b] Reduction yield 20 %. [c] Cf. Table 6.

An attempt was made recently to employ oxazolines as a chiral media to induce asymmetric Grignard additions to prochiral carbonyl compounds[36]. The 4-methoxy-2-methyloxazoline *(60)* was complexed with 0.3 equiv. of Grignard

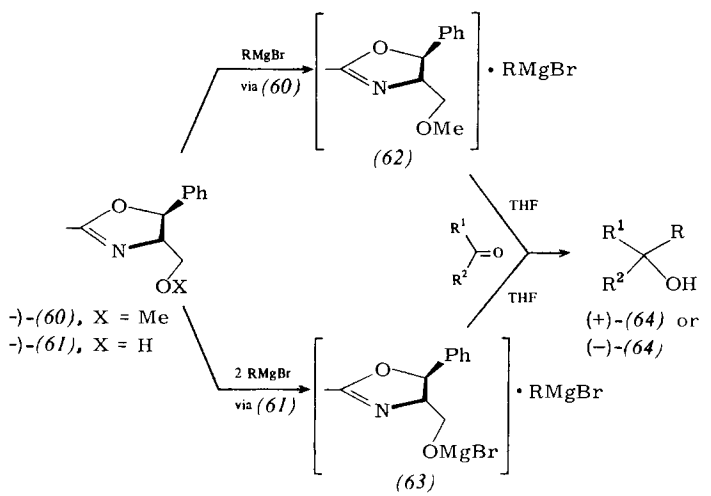


Table 8. Asymmetric additions of oxazoline-complexed Grignard reagents to carbonyl compounds.

Carbonyl cpd.	R in RMgBr	Oxazoline	$[\alpha]_D^{25}$ [a]	Config.	[%] [b]
EtCOPh	Me	*(60)*	+2.95	*R*	17
EtCOPh	Me	*(61)*	−4.30	*S*	25
MeCOEt	Ph	*(61)*	−2.45	*S*	9
c-C_6H_{11}COPh	Me	*(61)*	−2.13	*S*	11
c-C_6H_{11}COPh	Ph	*(61)*	−2.57	*S*	13
PhCHO	Me	*(61)*	+5.03	*R*	12
t-BuCHO	Ph	*(61)*	−0.58	*S*	21
t-BuCHO	Ph	*(60)*	−0.02	*S*	0.5

[a] Neat.
[b] ee = enantiomeric excess.

7. Aldehydes

A one-carbon homologation of Grignard reagents to aldehydes has been reported using 3,4,4-trimethyloxazolinium iodide *(66)*[39]. Addition of the Grignard reagent previously complexed with hexamethylphosphoric triamide gave the adduct *(67)* which was hydrolyzed to the aldehyde *(68)* in 50—90 % yield (Table 9). The starting oxazoline *(65)* was also transformed into its 2-deuterio derivative *(69)* and, after performing the same sequence of reactions, gave the C^1-deuterated aldehyde *(70)*. Unfortunately, alkyl Grignard reagents react poorly with *(66)*; the major side reaction is proton abstraction from C^2-H and the *N*-methyl group.

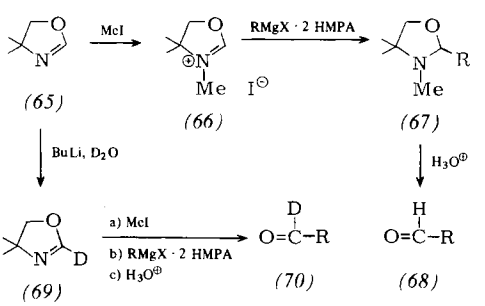
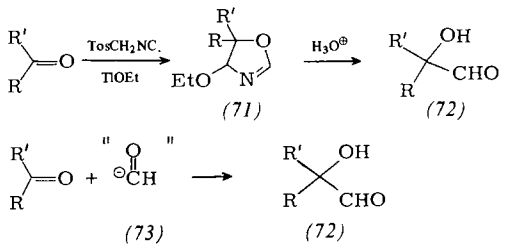


Table 9. Aldehydes *(68)* and *(70)* from Grignard addition to *N*-methyloxazolinium salts.

RMgX	Aldehyde	Yield [%]
PhMgCl	*(68)*, Benzaldehyde	77
o-$MeOC_6H_4MgBr$	*(68)*, *o*-Anisaldehyde	90
o-$MeOC_6H_4MgBr$	*(70)*, [D]-*o*-Anisaldehyde	70
PhC≡CMgBr	*(68)*, Phenylpropargyl aldehyde	51
PhCH=CHMgBr	*(68)*, Cinnamaldehyde	64
$PhCH_2MgCl$	*(68)*, Phenylacetaldehyde	87

A novel synthesis of 4-ethoxy-2-oxazolines *(71)* has led to a facile preparation of 2-hydroxy aldehydes *(72)* in monomeric form (Table 10)[40]. In this instance, the oxazoline ring serves as a "formyl anion" equivalent *(73)*[41].



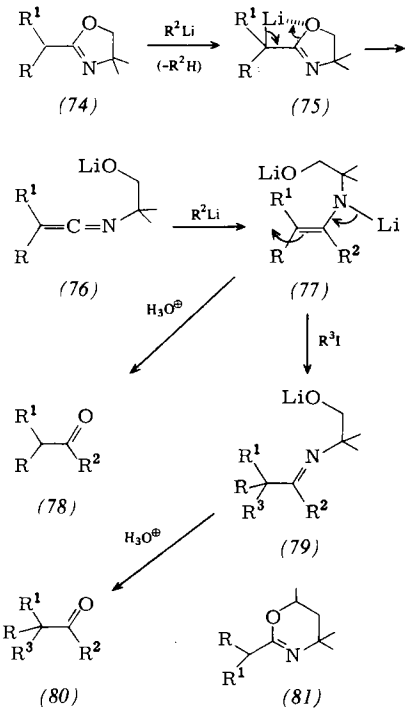
(71) *(72)* *(73)* *(72)*

Table 10. α-Hydroxy aldehydes *(72)* from carbonyl compounds.

R	R'	Yield [%]
—$(CH_2)_5$—		38
n-Pr	*n*-Pr	52
t-Bu	Me	70
Ph	Me	70
RR'CO = 3-cholestanone		70 (3α-ol only)

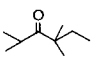
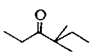
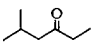
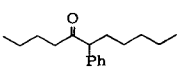
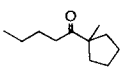
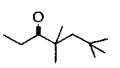
8. Ketones

The ready availability of 2-substituted oxazolines prompted *DuBois* and *Lion*[42] to develop a facile synthesis of hindered ketones based on previous studies with the dihydro-1,3-oxazine system *(81)*[43]. Advantage was taken of the reported[43] fact (since it is a lithioenamine) and undergoes alkylation once more to give *(79)*. Hydrolysis of the latter provides α-(quaternary alkyl) ketones *(80)* which may contain four different alkyl groups. A representative series of ketones is given in Table 11.



(74) *(75)* *(76)* *(77)* *(78)* *(79)* *(80)* *(81)*

Table 11. Unsymmetrical ketones from 2-oxazolines *(74)* [42] or dihydro-1,3-oxazines *(81)* [43].

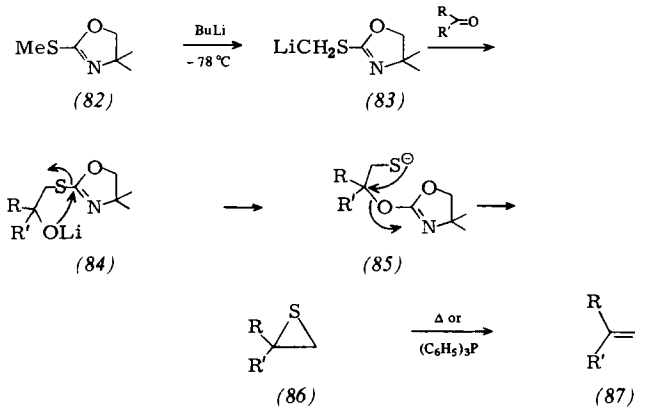
R in *(74)* or *(81)*	R^1	R^2	R^3	Ketone	Type	Yield [%]	Ref.
Me	Me	*i*-Pr	Et		*(80)*	96	[42]
Me	Et	Et	Me		*(80)*	74	[42]
Me	Me	Et	—		*(78)*	89	[42]
H	*i*-Pr	Et	—		*(78)*	83	[42]
Ph	*n*-Pent	*n*-Bu	—		*(78)*	77	[43]
—$(CH_2)_4$—		*n*-Bu	Me		*(80)*	63	[43]
Me	*neo*-Pent	Et	Me		*(80)*	65	[43]

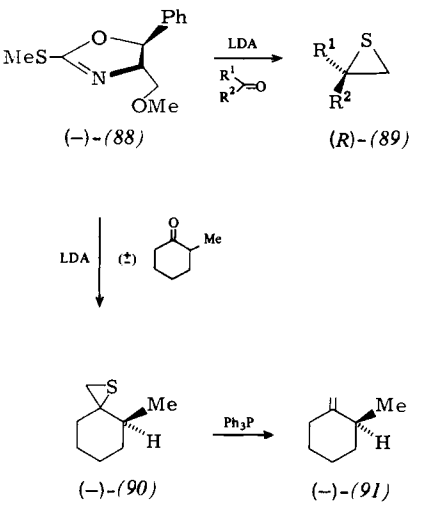
that tertiary lithium compounds of type *(75)* are unstable and readily rearrange to the ketenimines *(76)*. Addition of organolithium or Grignard reagents gave *(77)* which could be hydrolyzed to the unsymmetrical ketones *(78)* (Table 11). Alternatively, the intermediate *(77)* reacts with alkyl halides

9. Thiiranes and Olefins

A one-carbon homologation of carbonyl compounds to thiiranes *(86)* has been effected using the 2-(methylthio)oxazolines *(82)*[44]. The reaction leading to thiiranes is a "one-pot"

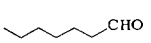
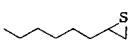
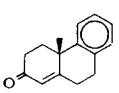
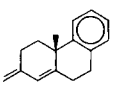
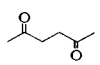
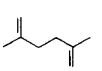
reaction which does not involve the isolation of intermediates *(84)* and *(85)* which can be converted directly into olefins *(87)*. Since the fragmentation-rearrangement sequence *(84)* → *(85)* → *(86)* does not take place until the reaction temperature exceeds −20 °C, it is possible to trap *(84)* with trimethylchlorosilane. Representative thiiranes and olefins are given in Table 12[46]. A similar reaction of thiazolines gave only poor yields[45].





fins were also shown to be obtainable when (±)-2-methylcyclohexanone was treated with the lithium salt of *(88)*. The resulting thiirane *(90)* ($[\alpha]_D^{25} = -0.42$) was desulfurized with triphenylphosphane to give the chiral olefin *(91)* in 30% ee.

Table 12. Thiiranes *(86)* and olefins *(87)* from 2-(methylthio)oxazolines *(82)* and carbonyl compounds.

Carbonyl cpd.	Thiirane	Yield [%]	Olefin	Yield [%]
		73		69
		78		
Ferrocene-carbaldehyde		68		
		66		
		61		65
	[a]			42
	[a]			48
	[a]			40

[a] The thiirane decomposes spontaneously to the olefin during workup.

9.1. Optically Active Thiiranes and Olefins

Application of the thiirane synthesis to chiral derivatives *(89)* has also been successfully implemented[47]. The oxazoline *(88)* was subjected to the same conditions as the achiral derivative and gave chiral thiiranes of 19—32% ee [examples: *(R)*-*(89)*, $R^1 = H$, $R^2 = n$-hexyl, ee = 21%; $R^1 = H$, R^2 = cyclohexyl, ee = 32%; $R^1 = H$, R^2 = phenyl, ee = 19%]. Chiral ole-

10. Aromatic Carboxylic Acids

10.1. *Via* Metalated Aryloxazolines

Since oxazolines react only poorly with Grignard reagents, a series of bromobenzoic acids *(92)* was converted into their oxazoline derivatives *(93)* and then transformed into the corresponding Grignard reagents *(94)*. Treatment with a variety

of electrophiles (E) was shown to give the elaborated benzoic acids *(95)* in good overall yield (Table 13)[48]. The reaction appears to be insensitive to steric effects and *ortho*-substituted benzoic acids are formed in good yields.

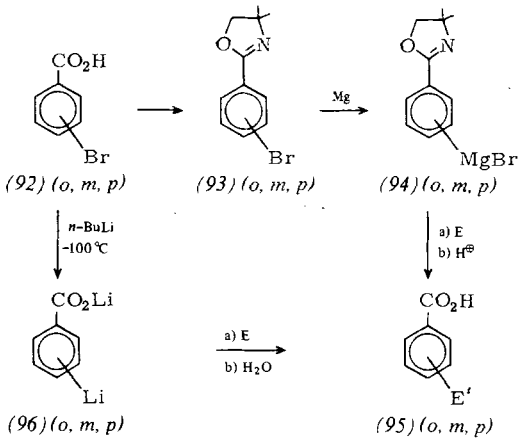
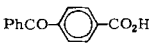
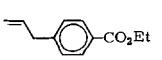
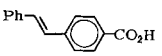
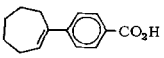
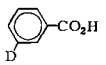
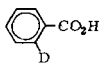
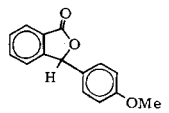


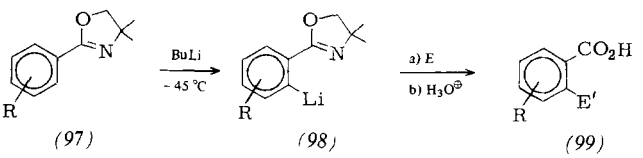
Table 13. Substituted aromatic acids *(95)* from aryloxazolines *(93)*. Yields are based on *(93)*.

Isomer of *(93)*	Electrophile E	Product	Yield [%]
para	Benzonitrile		81
para	Allyl bromide	 [a]	68
para	Styrene oxide		83
para	Cycloheptanone		80
meta	D_2O		86
ortho	D_2O		85
ortho	Cycloheptanone		80
ortho	*p*-Anisaldehyde		78

[a] Hydrolysis of *(94)* performed in 1.5 N H_2SO_4 in ethanol.

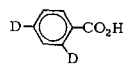
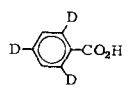
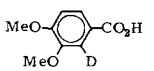
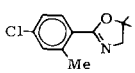
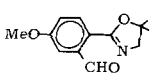
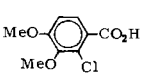
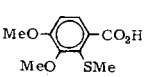
Recently *Parham*[49] described a similar technique. After successful metalation of bromobenzoic acids with *n*-butyllithium at −100 °C to their lithio derivatives *(96)*, addition of electrophiles also gave the substituted benzoic acids. Although the yields for both reaction types were good, their generality is limited by the availability of the appropriate bromo acids.

It has been recently observed by two research groups[50, 51] that aryloxazolines *(97)* are efficiently metalated to their *ortho*-lithio derivatives *(98)* which, as expected, may also be elaborated to substituted benzoic acids *(99)*. Some representative examples are given in Table 14. This metalation is very highly



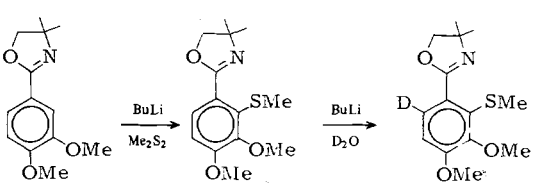
(97) (98) (99)

Table 14. Alkylation of (*ortho*-lithioaryl)oxazolines *(98)* to give *ortho*-substituted benzoic acids *(99)*.

No.	*(97)*, R	E	*(99)*	Yield [%]
1	4-D	D_2O		76
2	2,4-D_2	D_2O		74
3	3,4-$(MeO)_2$	D_2O		71
4	4-Cl	MeI		71 [a]
5	4-MeO	DMF		70 [a]
6	3,4-$(MeO)_2$	NCS		90
7	3,4-$(MeO)_2$	Me_2S_2		93

[a] Yields of oxazolines after addition of electrophile. These compounds were not hydrolyzed to the acids[50], although they would be expected to give benzoic acids in good yield.

regioselective in that *ortho*-lithiation occurs only at the position adjacent to the *meta* methoxy groups (examples 3, 6, and 7). Of particular significance is the fact that treatment of *(100)* with *n*-butyllithium followed by addition of dimethyl disulfide provides *(101)* in 94 % yield whereas a second equivalent of butyllithium now may be used to metalate the 6-position and another electrophile may be added, giving *(102)*[27]. This sequence illustrates the immense versatility of lithiated aryloxazolines and should provide a welcome addition to the classical approach to aromatic substitution.

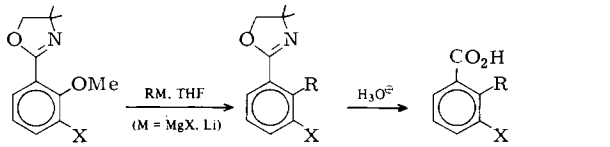


(100) (101) (102)

10.2. *Via* Methoxyaryloxazolines

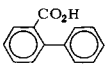
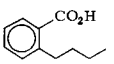
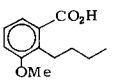
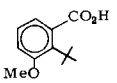
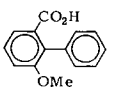
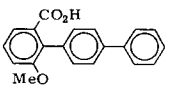
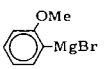
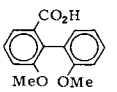
The above description of the synthetic utility of aryloxazolines has also been extended to nucleophilic additions. Thus,

2-(methoxyaryl)oxazolines, when treated with an organolithium reagent (−45 °C) or a Grignard reagent (25 °C), undergo facile methoxyl displacement giving substituted aryl oxazoline

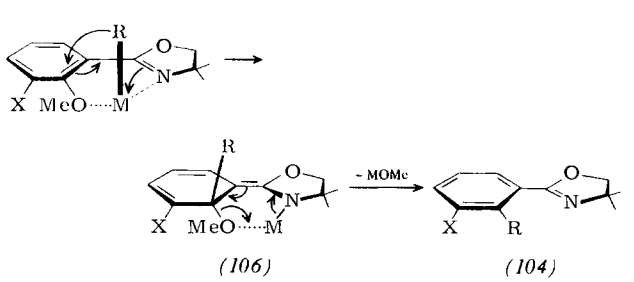


(103), X = H, MeO *(104)* *(105)*, X = H, MeO

Table 15. Nucleophilic aromatic substitution of 2-(methoxyaryl)oxazolines *(103)* to give substituted benzoic acids *(105)*.

X	RM	*(104)* Yield [%]	*(105)*	*(105)* Yield [%]
H	PhMgBr	95		75
H	*n*-BuMgCl	85		74
MeO	*n*-BuLi	98		85
MeO	*t*-BuLi	≈100		45
MeO	PhLi	≈100		70
MeO	*p*-Ph—PhLi	73		48
MeO		95		78

(104) in excellent yields. Hydrolysis provides the newly substituted alkyl (or aryl) benzoic acids *(105)* (Table 15)[52]. Although only a preliminary report has appeared concerning this method, further studies should demonstrate the novel and versatile approach to aromatic compounds so difficult or tedious to prepare by conventional routes[53]. The synthesis of unsymmetrical biaryls has always been a difficult task[54, 55]

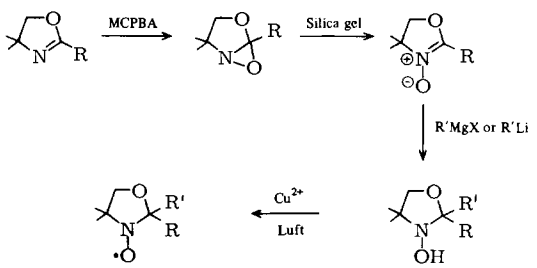


(106) *(104)*

and this new sequence may prove to be the method of choice in many instances. The nucleophilic substitution may be envisioned as occurring through a chelate-assisted addition of the organometallic to the aromatic ring furnishing the "metalated enamine" *(106)*. Elimination of metal methoxide provides the substituted aryloxazoline *(104)*.

11. Oxazolines as Spin Labels

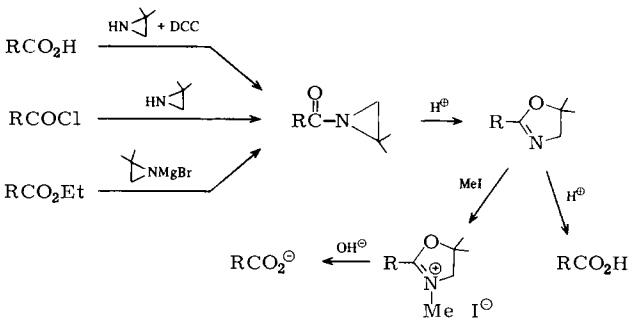
An elegant route to a series of useful biological probes was recently reported by *Keana*[56]. The process is outlined in Scheme 1. The flexibility of this approach allows the preparation of a large number of currently important compounds in yields comparable to other, less general methods.



Scheme 1. R = *n*-pentyl, R' = methyl, ethyl, or vinyl, MCPBA = *m*-chloroperbenzoic acid.

12. Oxazolines as Protecting Groups

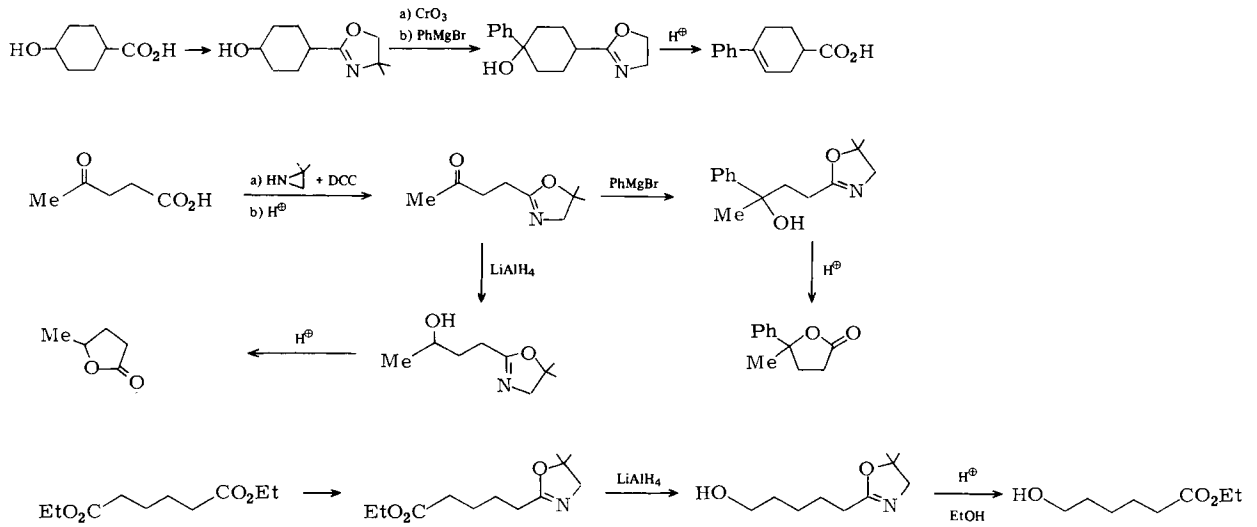
An examination of the preceding sections reveals a number of properties of the oxazoline ring that suggest it to be a valuable protecting group. It is inert to Grignard reagents,



Scheme 2. DCC = dicyclohexylcarbodiimide.

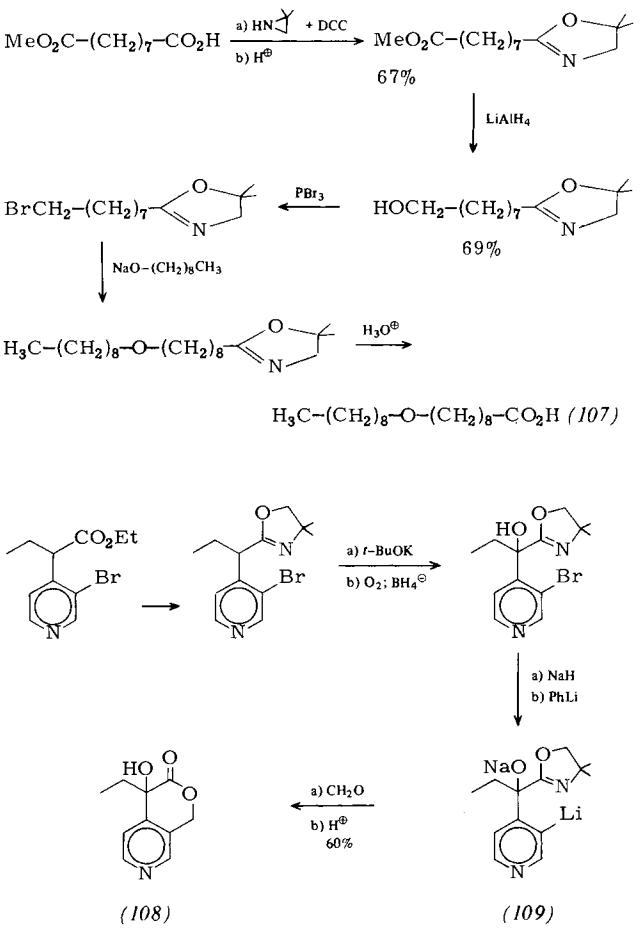
lithium tetrahydridoaluminate, organolithium reagents (when no α-protons are present on the 2-substituent), mild alkali, and mild acid. Furthermore, it may be hydrolytically removed under stronger acidic or basic conditions[48]. The remaining necessary condition for a protecting group, *i. e.* mild formation, is also fulfilled. Thus, a carboxyl function (acid, acid chloride, or ester) may be masked as the oxazoline by use of 2,2-dimethylaziridine. The various ways in which a carboxyl function may be protected and released are given in Scheme 2. Several examples of the use of the oxazoline as a protecting group are given in Scheme 3.

Recently, a structure proof for an unusual fatty acid *(107)* was performed using an oxazoline protecting group[57]. Application of the oxazoline masking group was reported in an



Scheme 3

approach to the CD-ring of the alkaloid Camptothecin *(108)*[58]. The presence of the oxazoline ring allowed the lithiopyridine derivative *(109)* to form cleanly and subsequent reaction with formaldehyde and acid produced the desired product.



13. Summary and Conclusions

The versatility of the simple heterocyclic system known as 2-oxazolines has been demonstrated by surveying the existing literature to date (October 15, 1975). It is difficult to imagine how so many years could have elapsed since the compounds were initially prepared[59] (1884!) before their synthetic usefulness was appreciated. One must therefore wonder how many other useful chemical properties are hidden in this and other well-known heterocyclic systems.

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Electro-Deprotection— Electrochemical Removal of Protecting Groups[**]

By V. G. Mairanovsky[*]

The reactions of electrochemical splitting may be successfully used for removal of protecting groups. Theoretical and preparative aspects of the method of electro-deprotection are discussed, and examples of its use are given. The removal often requires high potentials. The use of modified protecting groups ("inner activation") or of catalysts (electron carriers) which facilitate electron transfer against the standard potential gradient ("external activation"), can greatly increase the scope of the electrochemical method.

1. Introduction

Temporary blocking (protecting) of definite centers of a molecule which prevents them from undesirable change in the course of the reaction is a widely adopted method in many syntheses, especially in peptide and carbohydrate chemistry[2]. Removal of the protecting groups is usually carried out by more or less severe chemical treatment, frequently at higher temperatures and in the presence of acids or bases which may cause degradation or racemization.

As shown by recent investigations many protecting groups used in the synthesis of organic compounds can be removed by electrochemical reactions. Mild reaction conditions and the possibility of smooth variation in the strength of reagent (electrode) by merely changing its potential makes electrolysis a very attractive method for such conversions. In principle all reactions for the cathodic cleavage (electroreduction) of chemical bonds could be used.

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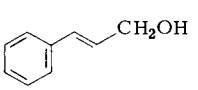
[**] Based on a report to the VIII All-Union Conference on Organic Electrochemistry (cf. also Ref. [1]).

2. Electrolysis Conditions—Influence of Solvent and pH Value

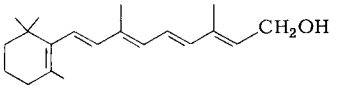
Although the first instances of cathodic bond cleavage (C—O in hydroxyketones[3], C—N in aminoketones and aminonitriles[4, 5], C—S in thiones[6]) were observed in solutions with a high content of proton donors, in many cases aprotic solvents seem to be more suitable[*]. Their high stability toward electroreduction permits working at as highly negative potentials as are required for the removal of most protecting groups. In addition, the low content of proton donors in the solution helps to decrease the rate of competitive protolytic reactions.

The possibility of competition between two chemical reactions—bond cleavage and protonation after an electron transfer—was apparently first noted in the reduction of β,γ-unsaturated alcohols: sorbyl alcohol *(1)*, cinnamyl alcohol *(2)*, and vitamin A *(3)*[8].

$H_3C-CH=CH-CH=CH-CH_2OH$ *(1)*

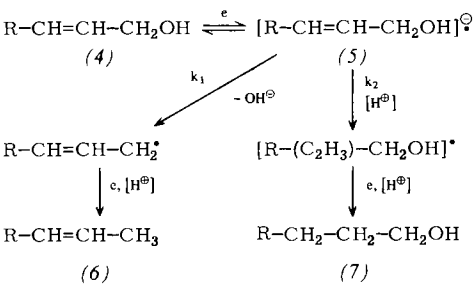


(2)



(3)

The negligible difference in half-wave potentials for the cathodic reduction of unsaturated alcohols of type *(4)* and the unsaturated hydrocarbons $R-CH=CH_2$ led us to the conclusion that the two reactions have a common intermediate product—namely, the radical anion *(5)* [Eq. (a)][8].



(a)

(6) *(7)*

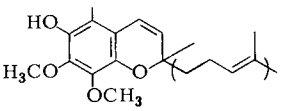
Predominant formation of the hydrocarbon *(6)* in the electrolysis of *(4)* in dimethylformamide (DMF) was ascribed to the higher rate of C—O bond cleavage in radical anion *(5)* compared to the rate of protonation under these conditions (DH = proton donor):

$$V_1 = k_1\,[(5)]$$
$$V_2 = k_2\,[(5)]\,[DH]$$

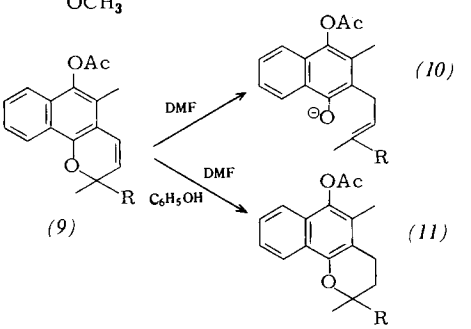
It was natural to expect that the increase of protonic activity of the solution be accompanied by an increase in V_2 and therefore that the yield of the desirable ("cleaved") product *(6)* would decrease: when $V_2 > V_1$ the formation of the saturated alcohol *(7)* should predominate.

[*] Apparently, *Given* and *Peover* were the first to observe the cleavage of a C—O bond in an aprotic medium during the electroreduction of 9,10-anthracenediol in dimethylformamide [7].

Such a mechanism, in fact, was found to be of common occurrence (see also Ref. [9]). Thus, in the electroreduction of ubichromenol *(8)* (inner ether of a substituted cinnamyl alcohol—cyclic isomer of ubiquinone) or naphthochromenol *(9)* [a similarly derived vitamin K derivative; reaction (b)] in DMF a corresponding hydroquinone derivative is formed in exceedingly large amounts, while the chromanol derivative was the main product of the electroreduction in the presence of proton donors; this could also be obtained in high yield[12].



(8)

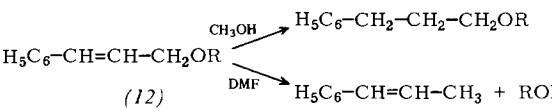


(b)

(9) *(10)* *(11)*

α,β-Unsaturated sulfones[13, 14], pyridine carbonitriles[15], benzoin and furoin[16], chloromaleic and chlorofumaric acids[17], 2,2-dichloronorbornane and its chloro-bromo analogs[18], as well as 4-(chlorostyryl)pyridines[19] and other compounds, were also reduced in this way.

A direct indication that the use of aprotic solvents is preferable in electroremoval of the protecting groups follows from a comparison of the reduction of cinnamyl ethers *(12)* in methanol[20] and in DMF: in methanol the cinnamyl moiety evidently cannot be used as a protecting group (hydrogenation of the ethylene bond is to be expected instead of C—O bond cleavage) but it can in DMF[21, 22].



(c)

(12)

It should be noted however that in some cases (for example in the removal of tosyl or benzoyl protecting groups) the use of an aprotic medium is not necessary. Protonation and cleavage reactions do not compete with each other here (see Sections 3.1 and 3.2). In contrast electroreduction of the C—N bond in α-aminoketones requires previous protonation of the nitrogen atom[23–27].

An important condition is maintaining the proper acidity (basicity) of the medium during electrolysis. For example, an increase in pH in the catholyte may not only change the direction of the reaction but also result in the undesirable removal of a protecting group, racemization *etc.* Monitoring and control of the pH during the electrolysis are beset with difficulties. Since the pH-meter reading can change by a few hundred mV after the current is switched on either the electrolysis must be interrupted during the pH-measurements[28] or a complicated arrangement must be resorted to which allows electrical isolation of the solutions in the electrolyzer and in the pH-meter cell[29].

Assuming that this effect is for the most part brought about by the drop in potential (iR) between the pH-meter electrodes we decreased the distance between them. We succeeded in almost completely eliminating the interferences, even in non-aqueous solvents, by using a special pH-meter sender. This differed from the usual arrangement in that one end of the electrolyte bridge of the reference electrode was in direct contact with the membrane of the glass electrode (Fig. 1).

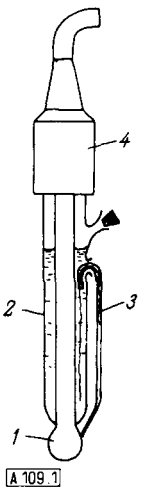


Fig. 1. Electrode sender for pH control during electrolysis. 1: glass electrode; 2: calomel electrode casing; 3: electrolytic bridge; 4: holder.

A pH-stat system[30] constructed with such a sender was used in most of our experiments on electro-deprotection; the working point mostly corresponded to the solvent (DMF) acidity. Moreover, the consumption of acid and current was recorded automatically, so we were able to determine continuously the number of electrons and protons consumed during the process. (A detailed description of the arrangement and examples of its use in studying the mechanism of electroorganic reactions is given in Ref. [30].)

Effective maintenance of the pH value necessitated vigorous stirring of the solution. Sometimes buffer components (*e.g.* phenol) were added to the solution to raise the efficiency of the system.

In other respects the conditions of electrolysis did not differ from those usually employed (mercury or lead cathode, glass frit or alundum diaphragm, potentiostat, bubbling of inert gas *etc.*). In some cases we were able to dispense with a diaphragm; it was found that performing the electrolysis under these conditions was not accompanied by large changes of pH, probably because of partial neutralization of the basic and acidic products formed at cathode and anode, respectively. To prevent alkalinization of the catholyte during electrolysis in a nonaqueous medium, *Saveant* and *Su Khac Binh*[111] have suggested carrying out the electrolysis without a diaphragm at a platinated Pt anode with hydrogen bubbling.

3. Electrochemical Removal of Protecting Groups

3.1. Removal of the Tosyl Group

In 1965 *Horner* and *Neumann*[31] discovered that the reduction of esters or amides of *p*-toluenesulfonic acid (TosOH) at a mercury cathode in methanol in the presence of tetramethylammonium chloride led to free alcohols (or amines) and toluenesulfinic acid in good yields (55—98 %). The process was carried out without control of potential; S—O and S—N bond cleavage was explained by the action of tetramethylammonium amalgam formed at the cathode. In later work[32, 33] a direct electrochemical reduction was proposed [Eqs. (d) and (e)].

$$p\text{-}H_3C\text{-}C_6H_4\text{-}SO_2\text{-}OR \xrightarrow{2\,e,\,[H^{\oplus}]} p\text{-}H_3C\text{-}C_6H_4\text{-}SO_2^{\ominus} + ROH \quad (d)$$

$$p\text{-}H_3C\text{-}C_6H_4\text{-}SO_2\text{-}NR'R'' \xrightarrow{2\,e,\,[H^{\oplus}]} p\text{-}H_3C\text{-}C_6H_4\text{-}SO_2^{\ominus} + R'R''NH \quad (e)$$

Contrary to the usual methods of tosyl cleavage the process was not complicated by side reactions and did not cause a marked decrease in optical purity, as observed in the cases of menthol, borneol and cholesterol derivatives.

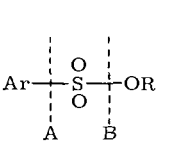
According to our investigations[34] the tosyl protecting group (Tos) in amino acids and aromatic or aliphatic amines and alcohols can also be cleaved in 70—90 % yield in an aprotic solvent (solution of $(Alkyl)_4NI$ in DMF). The ease of S—O and S—N bond cleavage decreases in the following sequence: Tos—O—Ar > Tos—O—Alkyl, Tos—NH—Ar > Tos—NH—Alkyl > Tos—NH—CH(Alkyl)—COOH[*].

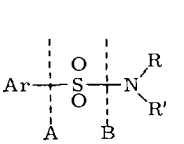
All these experiments show that it is possible to remove *O*-tosyl groups by electrolysis without affecting *N*-tosyl groups of amino acids and aliphatic amines. *Mann et al.* reported the possibility of using another aprotic solvent (acetonitrile) in the detosylation reactions[35, 36].

The formation of identical products during electrolysis in different solvents does not mean that the mechanisms of the reactions are identical. The demonstrated correlation between substituent constants and polarographic half-wave potentials in different media (DMF, dimethyl sulfoxide, acetonitrile[37] pyridine, benzonitrile[38], DMF in aqueous alcohol[39]) does not seem to be sufficiently informative.

On the contrary there are data indicating a significant influence of the experimental conditions (including the nature of the anion in the supporting electrolyte, and of the cathode material[35]) on the course of the electroreduction of arenesulfonates; the mechanism of the reaction evidently cannot be concluded with absolute certainty.

Detection of toluene during electroreduction of alkyl tosylates in acetonitrile led the authors[35] to conclude that two parallel reactions occur: the S—O bond cleavage (final products are alcohol and sulfinic acid) and C—S bond cleavage (the final products may be alcohol and toluene). The latter reaction was predominant when arenesulfonamides were reduced in aqueous, buffered solutions[40] [**].





[*] The $-E_{1/2}$ values (*vs* SCE) within the groups of substances mentioned fluctuated between 1.99 ± 0.03; 2.20 ± 0.06; 2.55 ± 0.08, 2.67 ± 0.04 V. In the case of *N*-tosyl-α-amino acids a "hydrogen" wave was observed in the polarogram, its $-E_{1/2}$ value lies between 2.1 and 2.3 V (cf. also *V. G. Mairanovsky* and *N. F. Loginova*, Bioorg. khim., in press).

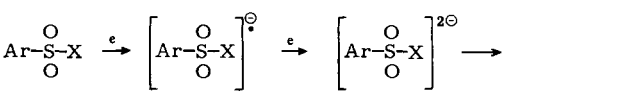
[**] There is evidence available that electroreduction of *N*-tosylamino acids in acid/alcohol medium does not lead to free amino acids [41].

Two such parallel reactions (routes A and B) can also be demonstrated in the case of homogeneous electron transfer to arenesulfonates and arenesulfonamides; thus, *e.g.* in the reduction of *N*-tosylamino acids or -peptides by Na in liquid ammonia[42], in the reduction of tosylates by naphthalenesodium[43] or in the reduction of tosylamides by arene radical anions in dimethoxyethane[44].

No cleavage of the C—S bond has been observed, however, in the electroreduction of ditosylates (Tos—O$(CH_2)_n$—O—Tos, $n=2$–6) in DMF[45] and of arenesulfonamides in acetonitrile[36]. Formation of toluene, which would indicate that the reaction followed "route A", was also not observed in our experiments on electroreduction in DMF[34].

We do not wish to dwell on the possible reasons for the above mentioned differences[*] but rather to discuss in more detail the frequently occurring case where the reaction proceeds predominantly *via* "route B"[31,34,36,45,46].

It is usually accepted that the S—X bond in arenesulfonates, arenesulfonamides and arylalkylsulfones is cleaved after the transfer of a second electron [eec mechanism Eq. (f)][**].

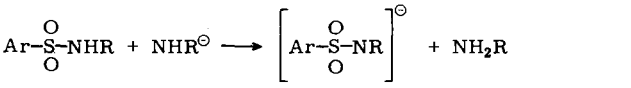


$$Ar\text{–}SO_2^{\ominus} + X^{\ominus} \qquad (f)$$

$$X^{\ominus} + DH \longrightarrow HX + D^{\ominus}$$

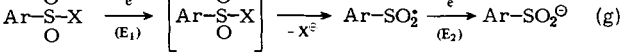
where X = OR [46], NR'R'' [36], Alkyl [47]
DH = proton donor (solvent or supporting electrolyte)

This equation also explains the formation of only one one-electron wave in the reduction of NH-tosylamides[36]; the decrease in wave height is attributed to deactivation of 50% of the initial compound (NH-acid) as a result of acid-base interaction with the anion $X^{\ominus}$ that is formed (here $NHR^{\ominus}$).



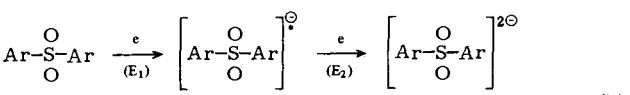
Nevertheless Eq. (f), which demands that the two electrons be transferred at exactly one and the same potential[46,47] (a common two-electron wave in a polarogram) does not seem convincing. In fact, proceeding from Eq. (f) it is difficult to explain why two separate one-electron transitions occur[46] in the case of diarylsulfones (when X = Ar) but not in the case of arylalkylsulfones (X = Alkyl). At the same time Eq. (f) predicts insufficient negative values of $E_{1/2}$ for the reduction of the radical anions $[Ar\text{—}SO_2\text{—}Alkyl]^{\ominus}$. Thus it gives $E_{1/2} = -2.36$ V[47] (or even still less negative values) *vs* SCE for $[H_5C_6\text{—}SO_2\text{—}CH_3]^{\ominus}$, while for $[H_5C_6\text{—}SO_2\text{—}C_6H_5]^{\ominus}$, which should be more easily reducible, a value of $E_{1/2} = -2.52$ V was measured[***]. The data obtained in the experiments on delayed homogeneous electron transfer against a standard potential gradient provide further evidence against Eq. (f) (see Section 4.2 and Table 1).

The following scheme of reduction [Eq. (g)] seems the more likely (ece mechanism):



$$(g)$$

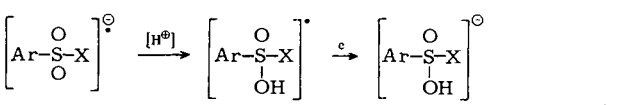
Here $E_2 > E_1$[*]; accordingly a two-electron wave is to be expected in the polarogram. The radical anion $[Ar\text{—}SO_2\text{—}X]^{\ominus}$ quickly dissociates when X = OR, NR'R'' or Alkyl; when $X = C_6H_5$ dissociation does not take place on the polarographic time scale:



$$(h)$$

In Eq. (h) $E_2 < E_1$; one can observe two one-electron waves in the polarogram.

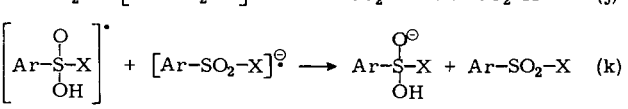
In contrast to a number of other cases [see Section 2, Eqs. (a)—(c)] electroreduction of tosyl derivatives in a protonic medium (methanol[31]) leads exclusively to formation of cleavage products, because the stepwise protonation of the radical anion $[Ar\text{—}SO_2\text{—}X]^{\ominus}$ (contrary to Eq. (a)) likewise leads to cleavage [Eq. (i)].



$$(i)$$

In addition one should take into consideration volume reactions such as (j) and (k).

$$Ar\text{–}SO_2^{\bullet} + [Ar\text{–}SO_2\text{–}X]^{\ominus} \longrightarrow Ar\text{–}SO_2^{\ominus} + Ar\text{–}SO_2\text{–}X \qquad (j)$$



$$(k)$$

The electrolytic method of removing tosyl groups has already been applied to the synthesis of *cis*- and *trans*-4-mercapto-L-prolines[48]. Sensitivity of the pyrrolidine ring in proline towards acid media and the instability of the protecting group on sulfur under conditions of catalytic hydrogenolysis limited the use of chemical methods to remove a tosyl group. Recently, Japanese authors[49,50] showed the possibility of reducing the cost of the procedure (a mercury electrode was replaced by a lead electrode and $K^{\oplus}$ and $Na^{\oplus}$ cations were used instead of tetraalkylammonium cations) and conducted the electrolysis of *N*-tosyl amino acids in aqueous methanol on a 10^1-gram scale[50]. The necessity of strictly maintaining a pH value of 11 during the experiment was especially emphasized; the authors used an automatic titrator for this purpose. When the electrolysis was performed without pH control the yield dropped by more than half and racemization took place[50].

Cox and *Ozment*[112] and *Horner* and *Meyer*[113] have demonstrated for the case of diarylsulfones a reaction mechanism which differs from the mechanism proposed by us [Eqs. (g) and (i)] in that it does not include cleavage of the radical anion.

[*] *R. Gerdil* [46] recently attempted to explain the different contributions of processes "A" and "B" by their dependence on the proton donor properties of the medium.

[**] e = electron transfer, c = chemical stage (cleavage).

[***] This $E_{1/2}$ value is taken from Ref. [46] and calculated relative to SCE.

[*] $E_2 > E_1$ means that potential E_2 is less negative than E_1.

3.2. Removal of the Benzoyl Group

Information on the polarographic activity of the amides and esters of benzoic acid (Bz—NH_2 and Bz—OR) first appeared in the late fifties[51, 52]. In connection with the problem of removing protecting groups *Horner et al.* pointed out the possibility of reducing benzoyl derivatives electrochemically[31, 33]. Electrolysis of esters and amides in 1 M tetramethylammonium bromide in methanol afforded alcohols or amines in 60—90% yield and benzyl alcohol (in approximately equivalent amounts).

$$H_5C_6{-}CO{-}NR'R'' \xrightarrow{4\,e,\,4\,[H^{\oplus}]} H_5C_6{-}CH_2OH + R'R''NH \qquad (l)$$

$$H_5C_6{-}CO{-}OR \xrightarrow{4\,e,\,4\,[H^{\oplus}]} H_5C_6{-}CH_2OH + ROH \qquad (m)$$

It has been found that benzoyl derivatives are slightly more difficult to reduce than tosyl derivatives[33][*]; Eq. (n) shows the possibility of selectively removing the tosyl protecting group in presence of the *p*-anisoyl (*p*-methoxybenzoyl) group[33].

$$p\text{-}H_3CO{-}C_6H_4{-}CO{-}NH{-}(CH_2)_4{-}\underset{\displaystyle -2.4\ V}{\underset{\uparrow}{CH}}{-}NH{-}\underset{\displaystyle -2.15\ V}{\underset{\uparrow}{Tos}} \xrightarrow[-\,Tos^{\ominus}]{2\,e,\,[H^{\oplus}]} \begin{matrix} COOH \\ | \\ p\text{-}H_3CO{-}C_6H_4{-}CO{-}NH{-}(CH_2)_4{-}CH{-}NH_2 \end{matrix} \qquad (n)$$

Horner's data for the electrochemical cleavage of C—N bonds confirms the results recently obtained in a polarographic study of benzamide and its derivatives in protonic media[53–57].

In contrast to literature data[58] we established that methyl benzoate and benzamide can also be reduced in aprotic media, the first stage being a one-electron transfer[21] leading to relatively highly stable radical anions[59]. Nevertheless, during the electrolysis of β-D-methyl-2-benzoyl-4,6-*O*-benzylidene-galactopyranoside *(13)* [see Eq. (q)] in DMF at the potential of the first wave (generation of a benzoyl radical anion), it was observed that the second benzoate wave gradually disappeared, thus indicating transformation of the radical anion in the solution. Such a behavior is typical for ece-processes. Formation of the debenzoylated carbohydrate *(14)* during the electrolysis indicates that one of the chemical stages is cleavage of a C—O bond [Eq. (o)].

$$Bz{-}OR \xrightarrow{e} [Bz{-}OR]^{\ominus\bullet} \longrightarrow RO^{\ominus} + Bz^{\bullet} \longrightarrow \cdots \qquad (o)$$

$$Bz = H_5C_6{-}CO \qquad\qquad RO^{\ominus} \xrightarrow{[H^{\oplus}]} ROH$$

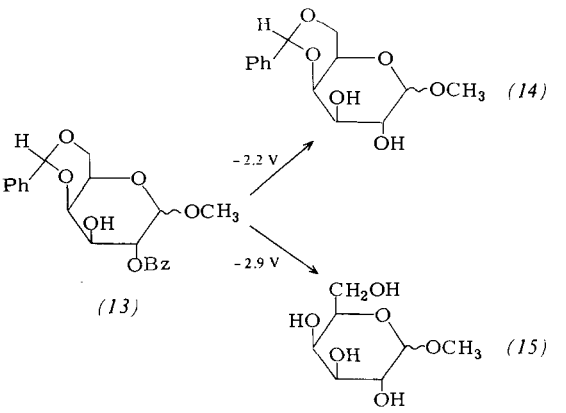
Like the tosyl radical, on electroreduction the benzoyl radical Bz$^{\bullet}$ can accept an electron either from the electrode or from the benzoate radical anion $[BzOR]^{\ominus\bullet}$; in principle the radical can still also undergo other reactions (dimerization, abstraction of H$^{\bullet}$ from the medium, *etc.*). The reactions of the benzoyl derivatives, like those of the tosyl derivatives, do not change on going over to the use of protonic media (cf. Ref. [33]). This means that the C—O bond may also cleave after the protonation [cf. Eq. (p) and Eqs. (i) and (k)].

[*] We have found that this is not the case in DMF (see Table 2).

$$[H_5C_6{-}CO{-}OR]^{\ominus\bullet} \xrightarrow{[H^{\oplus}]} \left[H_5C_6{-}C(OH)(OR)\right]^{\bullet} \xrightarrow{e} \left[H_5C_6{-}C(OH)(OR)\right]^{\ominus} \qquad (p)$$

$$\xrightarrow[-\,RO^{\ominus}]{} H_5C_6{-}CHO \xrightarrow{2e,\,2\,[H^{\oplus}]} H_5C_6{-}CH_2OH$$

Electrochemical removal of the benzoyl protecting group from the carbohydrate *(13)* in DMF proceeds in good yield and without attack at the benzylidene group[60]. If both groups are to be removed simultaneously from the carbohydrate, then a more negative potential must be chosen for the electrolysis[60].



(q)

3.3. Removal of Trityl, Benzhydryl, Benzyl, Phenyl, and Cinnamyl Groups

The trityl (triphenylmethyl), benzhydryl (diphenylmethyl), benzyl, and phenyl groups are used for the protection of hydroxyl, amino, and carboxyl groups as well as phosphoric

$$H_{31}C_{15}{-}CO{-}NH{-}CH_2{-}CH_2{-}O{-}Cin \xrightarrow{2e,\,2\,[H^{\oplus}]} H_{31}C_{15}{-}CO{-}NH{-}CH_2{-}CH_2OH + Cin{-}H \qquad (r)$$

(16)

$$H_{27}C_{13}{-}CH{=}CH{-}\underset{\displaystyle Cin{-}O}{CH}{-}\underset{\displaystyle NH{-}CO{-}C_{15}H_{31}}{CH}{-}CH_2{-}O{-}Cin \xrightarrow{4\,e,\,4\,[H^{\oplus}]} H_{27}C_{13}{-}CH{=}CH{-}\underset{\displaystyle OH}{CH}{-}\underset{\displaystyle NH{-}CO{-}C_{15}H_{31}}{CH}{-}CH_2OH + 2\ Cin{-}H \qquad (s)$$

(17)

$$H_{31}C_{15}{-}CO{-}NH{-}CH_2{-}CH_2{-}O{-}Trt \xrightarrow{2\,e,\,2\,[H^{\oplus}]} H_{31}C_{15}{-}CO{-}NH{-}CH_2{-}CH_2OH + HTrt \qquad (t)$$

(16)

$$(Bzl{-}O)_3PO \xrightarrow{2\,e,\,[H^{\oplus}]} (Bzl{-}O)_2\overset{\displaystyle O}{\overset{\|}{P}}{-}O^{\ominus} + H_5C_6{-}CH_3 \qquad (u)$$

$$(o\text{-}H_3C{-}C_6H_4{-}O)_3PO \xrightarrow{2\,e,\,[H^{\oplus}]} (o\text{-}H_3C{-}C_6H_4{-}O)_2\overset{\displaystyle O}{\overset{\|}{P}}{-}O^{\ominus} + H_5C_6{-}CH_3 \qquad (v)$$

$$H_{31}C_{15}{-}CO{-}O{-}Bzl \xrightarrow{2\,e,\,2\,[H^{\oplus}]} H_{31}C_{15}{-}COOH + H_5C_6{-}CH_3 \qquad (w)$$

(18)

$$AcNH{-}CH_2{-}CO{-}O{-}C_6H_5 \xrightarrow{2\,e,\,2\,[H^{\oplus}]} AcNH{-}CH_2{-}COOH + C_6H_6 \qquad (x)$$

(19)

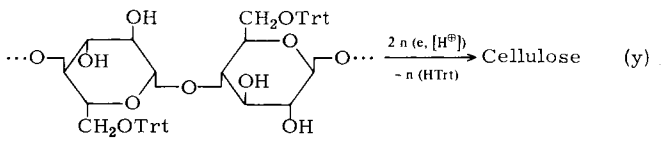
Cin = $H_5C_6{-}CH{=}CH{-}CH_2$; Bzl = $H_5C_6{-}CH_2$; Trt = $(C_6H_5)_3C$

acid esters; we suggested the cinnamyl group (Cin, see Section 4.1) be used for the blocking of the hydroxyl group[61].

According to polarographic measurements cinnamyl[21,8] and trityl ethers[62], benzyl and phenyl phosphates[63,64], as well as trityl, benzhydryl, benzyl, and phenyl esters of carboxylic acids[65,66] are electrochemically active in the supporting electrolyte (0.04 M tetraethylammonium iodide in anhydrous or 95% aqueous DMF). All of these protecting groups can be removed under the conditions of preparative electrolysis.

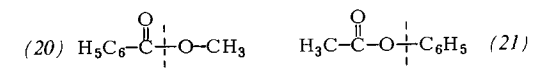
Several examples of such transformations, *e.g.* with derivatives of *N*-(2-hydroxyethyl)palmitamide *(16)*, *erythro*-*N*-palmitoylsphingosine *(17)* are given in equations (r)—(x); the yields of the products were 70—90%[61-65].

The preparation of cellulose from 6-*O*-tritylcellulose[1] can also serve as an example of electrochemical removal of the trityl protecting group [Eq. (y)]. The electrolysis was carried out with 0.1 M tetraethylammonium iodide in DMF. Free cellulose, which is very sparingly soluble in this solvent, precipitated out immediately it was formed; no decomposition products were observed. Electro-deprotection is very promising for use in the synthesis of modified polysaccharides.



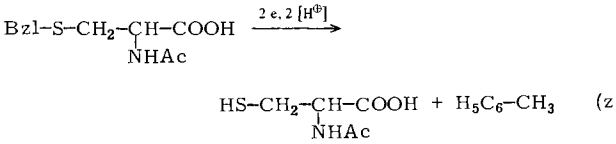
(y)

The reduction of ethers (Eqs. (r)—(t)) proceeds according to the mechanism given in Eq. (a) (see Section 2). It must be pointed out however that the residues of other unsaturated alcohols investigated in Refs. [8, 9] may be also be used as protecting groups.


(20) *(21)*

Interest attaches to the difference in behavior of the esters of aromatic and aliphatic carboxylic acids, *e.g.* isomeric methyl benzoate *(20)* and phenyl acetate *(21)*[66]. The sites of cleavage are indicated. Compound *(21)* is reduced at a potential *ca.* 0.6 V more negative than that at which *(20)* is reduced and without separation of the one-electron stage (formation of the radical anion) from the following stages. The different behavior of *(20)* and *(21)* can be rationalized on a quantum mechanical basis (position of the LUMO, degree of charge delocalization in the radical anion, *etc.*). As an estimation of the bond energies shows[66], the site of bond cleavage in *(21)* does not coincide with the least stable bond of the molecule in the ground state.

Benzyl derivatives of aliphatic alcohols are not reduced below the discharge potential of tetraethylammonium iodide in DMF (*ca.* −2.9 V *vs* SCE)[*]. At the same time we found that alkylbenzyl sulfides[68] are polarographically active due to the electrochemical cleavage of the C—S bond[**]. Thus electrolysis of *N*-acetyl-*S*-benzylcysteine results in formation of *N*-acetylcysteine in good yield (82%) [Eq. (z)].


(z)

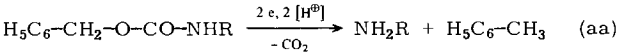
The electrochemical method for removal of the *S*-benzyl protecting group is especially promising for preparation of complicated peptides, as chemical methods often lead to undesirable side reactions (see *e.g.* Ref. [71]).

According to *Horner*'s and *Neumann*'s findings[31], which have been confirmed by other authors[48,49], the *S*-benzyl protecting group is not removed by electroreduction in methanol. Evidently other reactions of type (t)—(y), which require high cathodic potentials, cannot be carried out in this solvent. In the reactions (r) and (s) there is the danger of possible competitive protonation of an intermediate radical anion in methanol in accordance with Eq. (a).

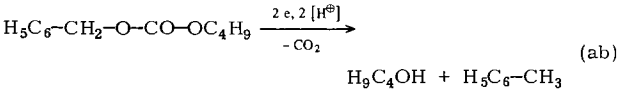
3.4. Removal of the Benzyloxycarbonyl Group

The benzyloxycarbonyl group (Z) is one of the most important groups for blocking the amino function, *e.g.* in peptide syntheses[72]. Chemical methods cannot always be used for its removal; this is so *e.g.* in the synthesis of some complicated polyfunctional compounds (*vide infra*).

It has already been reported that the *N*-benzyloxycarbonyl group cannot be removed by electrolysis in methanol solution[31,48,49]. We succeeded in removing this protecting group in good yield (70—80%) however by electroreduction in DMF at a high negative potential[73]. The reaction, which is revealed in the polarogram by a rise in current before discharge of the supporting electrolyte, can be formulated as in Eq. (aa) (CO_2 reduction is not included in the equation of the reaction).


(aa)

Electrolysis can also be used for removal of the Z protecting group from hydroxyl and thiol groups. Thus, in the reduction of Z-protected butanol equivalent amounts of butanol (70%) and toluene are obtained[68].

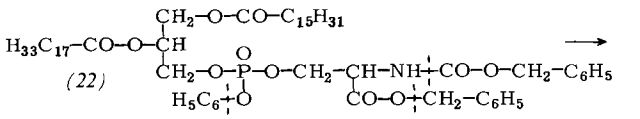

(ab)

The reduction of *S*-benzyloxycarbonylcysteine gives cysteine; the ease of removal of the protecting group increases in the series: amine < alcohol < thiol ($E_{1/2}$ of the Z-derivatives of *n*-butylamine, *n*-butanol and cysteine are −2.9, −2.7 and −2.62 V, resp., *vs* SCE). The removal of the *N*-benzyloxycarbonyl group from amino acids in DMF was not accompanied by marked racemization[1].

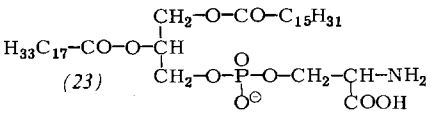
The electrochemical method for removal of the benzyloxycarbonyl group was used in the synthesis of glycerol phosphatides containing residues of unsaturated acids[64,74], which naturally do not permit removal of the protecting group by catalytic hydrogenolysis. An example is the preparation of

[*] In DMF with $(n\text{-}C_4H_9)_4N^{\oplus}ClO_4^{\ominus}$ as supporting electrolyte, alkyl benzyl ethers are first reduced shortly before discharge of the electrolyte [67]; thus *e.g.* butyl benzyl ether has a half-wave potential of *ca.* −3.1 V in this solution.

[**] The electrochemical reduction of diaryl-, arylalkyl-, dibenzyl- [69], and arylbenzhydryl sulfides [70] has also been reported.



(22) (ac)

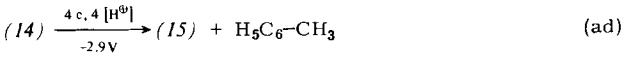


(23)

the phosphatidylserine derivative *(23)* from compound *(22)*[74], in which all three protecting groups were removed by electroreduction at −2.9 V in the final stage of the synthesis.

3.5. Removal of the Benzylidene Group

This group, which is widely used in carbohydrate chemistry for blocking hydroxyl groups, is usually removed by acid hydrolysis or catalytic hydrogenation. We found that benzylidene derivatives of carbohydrates can be reduced polarographically in DMF at a potential at which discharge of the supporting electrolyte (0.04 M tetraethylammoniumiodide) begins. Preparative electrolysis of β-D-methyl-4,6-*O*-benzylidene-galactopyranoside *(14)* yielded the methylgalactoside *(15)* and toluene [Eq. (ad), cf. Eq. (q)].



(ad)

It is interesting to note that C—O bond cleavage during the electroremoval of protecting groups from carbohydrates occurs at rather less negative potentials than in the case of protected aliphatic alcohols[60].

4. Electro-deprotection with Activation

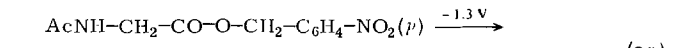
As can be seen from the previous Sections electrochemical removal of protecting groups requires rather high cathodic potentials (from *ca.* −2.0 to *ca.* −3.0 V *vs* SCE). It should be possible to extend the working range to less negative potentials and thus increase the scope of the method.

4.1. Directed Modification of Protecting Groups ("Inner Activation")

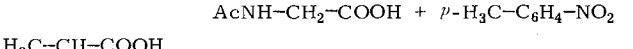
This problem could be solved in principle by increasing the electron affinity of the protecting group by introduction or elongation of a conjugated chain. If the reaction proceeds *via* formation of a relatively stable radical anion $[R—CH{=}CH—X]^{\ominus}$ [Eq. (a)], the ease of removal of the protecting group should compare to a first approximation with the ease of reduction of the corresponding unsaturated hydrocarbon. The dependence of the ease of reduction of unsaturated hydrocarbon on the parameters of the π-electron system (aromatic[75,76] or linear conjugated[77]) is described by known quantum mechanical correlations. An example is the use of the cinnamyl moiety $C_6H_5CH{=}CHCH_2$ instead of the benzyl moiety $C_6H_5CH_2$[61] for blocking the hydroxyl group: the former is removed smoothly at −2.5 V (*vs* SCE) while the latter remains secure until discharge of the supporting electrolyte (see however Footnote [*] in Section 3.3).

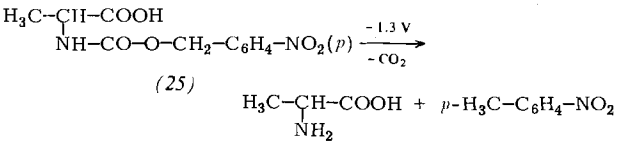
A variant of this activation method is the introduction of electron acceptors (A) at definite sites of the protecting group[78]. Taking into consideration the activating effect of a nitro group on the reductive splitting of halogen, as was observed in nitrohaloalkanes[79] and later in nitrohalobenzenes[80–85], we tested the nitro group[78,86] as activating substituent A.

The possibility of removing nitro-substituted protecting groups by reduction at the potentials of the first polarographic wave of the nitro group was first established in the case of the *p*-nitrobenzyl ester of *N*-acetylglycine *(24)*, *p*-nitrobenzyloxycarbonylalanine *(25)*, and *N*-(*o*-nitrophenylsulfenyl)-phenylalanine *(26)*. In order to avoid decomposition of the substance by attendant bases the electrolysis was carried out with pH-control at the "pH" of DMF. In all cases the protecting group could be removed and the corresponding amino acid was formed in good yield [Eqs. (ae)—(ag)][78].

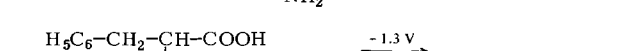


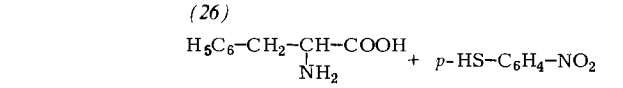
(24) (ae)



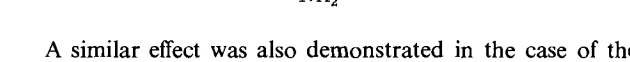


(25) (af)

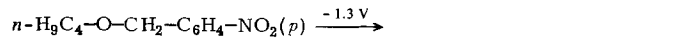




(26) (ag)



A similar effect was also demonstrated in the case of the *O*-benzyl group[1,67]. As in the activation by lengthening of a conjugated system (benzyl → cinnamyl, *vide supra*) introduction of a *p*-nitro substituent shifts the potential necessary for removal of the protecting group into an accessible range; in the case of the butyl derivative *(27)* $E_{1/2}$ is shifted more than 1.8 V. The yield of butanol is 60%. The electrolysis was performed at the "pH" of DMF.



(27) (ah)

In principle the mechanism of reactions (ae)—(ah) does not differ from the previously studied reduction of nitrohaloarenes[81,82]. However, our experiments on the use of cyclic voltammetry showed that the radical anions $[X—Ar—NO_2]^{\ominus}$ formed here are much more stable (rate constant of decomposition $<0.1\ s^{-1}$). The slow decrease in current during electroreduction of nitro compounds at the potentials of the first wave of the nitro group should be noted. It is evidently connected with the participation of radical anions [*e.g.* $[H_3C—C_6H_4—NO_2]$ in Eq. (ah)] in homogeneous electron transfer reactions which regenerate a neutral compound (nitrotoluene). The starting substance *(27)*, oxygen, and any other impurities present in the solution, can all serve as electron acceptors in such a catalytic conversion.

Besides the nitro group other electron accepting substituents (carbonyl, nitrile, halogen, *etc.*) can also be used as activating groups. The activating effect of a nitrile group manifests itself

by the easier removal of halogen from haloarenecarbonitriles; for instance, $E_{1/2}$ of chlorobenzene in DMF is *ca.* −2.8 V, and that of *p*-chlorobenzonitrile is −1.93 V (*vs* SCE; calculated from the data described in Ref. [87]). Similarly the *p*-cyanotoluenesulfonyl protecting group is removed at a much less negative potential than the toluenesulfonyl group[36].

The activating effect of halogens is particularly well revealed in the haloethoxy and haloethoxycarbonyl groups[88]. Examples of the ready removal of such protecting groups by electroreduction in methanol with 0.1 M $LiClO_4$ are given in Equations (ai)—(ao). The potentials are referred to SCE; the yields are 50—100 %[88].

$$H_5C_6{-}CO{-}O{-}CH_2{-}CHCl_2 \xrightarrow{-1.85\ V} H_5C_6{-}COOH \qquad (ai)$$

$$H_5C_6{-}CO{-}O{-}CH_2{-}CCl_3 \xrightarrow{-1.65\ V} H_5C_6{-}COOH \qquad (aj)$$

$$H_5C_6{-}CO{-}O{-}CH_2{-}CBr_3 \xrightarrow{-0.7\ V} H_5C_6{-}COOH \qquad (ak)$$

$$p\text{-}H_3C{-}C_6H_4{-}NH{-}CO{-}O{-}CH_2{-}CCl_3 \xrightarrow{-1.7\ V} p\text{-}H_3C{-}C_6H_4{-}NH_2 \qquad (al)$$

$$p\text{-}H_3C{-}C_6H_4{-}NH{-}CO{-}O{-}CH_2{-}CHCl_2 \xrightarrow{-2.15\ V} p\text{-}H_3C{-}C_6H_4{-}NH_2 \qquad (am)$$

$$H_5C_6{-}CH_2{-}O{-}CO{-}O{-}CH_2{-}CCl_3 \xrightarrow{-1.50\ V} H_5C_6{-}CH_2OH \qquad (an)$$

$$H_5C_6{-}CH_2{-}S{-}CO{-}O{-}CH_2{-}CCl_3 \xrightarrow{-1.50\ V} H_5C_6{-}CH_2SH \qquad (ao)$$

In these cases activator and protecting group are removed together. It must be pointed out that transformations (ai)—(ao) are similar to the electroreduction of vicinal haloethanes with different halogens[89] and of haloalcohols[90]. The homogeneous reduction of 2,2,2-trifluoroethyl ethers with naphthalenesodium proceeds in much the same way[91].

$$RO{-}CH_2{-}CF_3 \xrightarrow{C_{10}H_8^{\ominus},\ [H^{\oplus}]} ROH + H_2C{=}CF_2 + F^{\ominus} \qquad (ap)$$

One can consider that the scheme of "conjugated cleavage of halogens" proposed by *Feoktistov et al.*[89] may also be applied to the reactions (ai)—(ao), *i.e.* they may proceed *via* a concerted mechanism.

In a detailed interpretation of the reaction mechanism the formation of small amounts of dichloro from trichloro compounds [6% and 26%, reactions (aj) and (an)] observed by *Semmelhack* and *Heinsohn*[88] must be taken into consideration. The content of dichloro compounds changes slightly depending on the solvent (MeOH or DMF) and type of acid employed (acetic or trifluoroacetic).

$$\begin{array}{l} H_5C_6{-}CO{-}O^{\ominus} + H_2C{=}CCl_2 \qquad (aq) \\ \uparrow\ 2\ e,\ -Cl^{\ominus} \\ H_5C_6{-}CO{-}O{-}CH_2{-}CCl_3 \\ \downarrow\ 2\ e,\ [H^{\oplus}],\ -Cl^{\ominus} \\ H_5C_6{-}CO{-}O{-}CH_2{-}CHCl_2 \qquad (ar) \end{array}$$

These data indicate that here the cleavage of the C—O bond [Eq. (aq)] and protonation of the radical anion [Eq. (ar)] are not competitive reactions with participation of one and the same species [cf. Eq. (a)]. On the contrary, in view of the results of an investigation by *Feoktistov et al.* on the electrochemical[92–95] reduction of polyhaloethanes an alternative explanation can be suggested: whether the reaction proceeds according to Eq. (aq) or (ar) depends on the conformation of the participating species. [According to Refs. [92–94] Eq. (ar) can be ascribed to the reduction of the *gauche* conformer.]

Independently of the method (introduction of a conjugated system or electron acceptor) modification of a protecting group presents an opportunity to decrease the potential necessary for the bond cleavage. The opening of the bond should be practically irreversible and proceed rapidly in comparison to the competing deactivation of the radical anion by protonation *etc.* If these conditions are not fulfilled the protecting group may not be removed at all on account of its increased electron-acceptor properties. Thus the *p*- and *o*-nitrotoluenesulfonyl derivatives of glycine and *n*-butanol could not be split electrochemically on the preparative scale with pH control (at "pH" of DMF)[1]. As comparative experiments have shown (storage of the substance in basic DMF solution) the formation of small amounts of butanol (up to 20 %, GLC) during the electrolysis of butyl *p*-nitrotoluenesulfonate without pH-control is connected with the action of strong bases formed in the cathodic space during the electrolysis.

The electroreduction of *p*-nitrobenzenesulfonamides in DMF has recently been studied in detail by *Asirvatham* and *Hawley*[96]. S—N bond cleavage was found not to occur either, and the authors suggested that removal of a hydrogen atom takes place in the case of primary and secondary amides:

$$p\text{-}O_2N{-}C_6H_4{-}SO_2{-}NHR \overset{e}{\rightleftharpoons} \left[p\text{-}O_2N{-}C_6H_4{-}SO_2{-}NHR\right]^{\ominus\bullet} \xrightarrow[-H^{\bullet}]{} p\text{-}O_2N{-}C_6H_4{-}SO_2{-}NR^{\ominus} \quad \text{etc.} \qquad (as)$$

The polarographic activity of trifluoroacetates could be ascribed to cleavage of a C—O bond with formation of trifluoroethanol and free alcohol in a four-electron process[86]; however, preparative electrolysis at the "pH" of DMF showed it not to be connected with the removal of a trifluoroacetyl protecting group but rather with partial defluorination[1,97].

$$F_3C{-}CO{-}O{-}C_4H_9 \xrightarrow{4\ e,\ 2\ [H^{\oplus}]} H_2FC{-}CO{-}O{-}C_4H_9 + 2\ F^{\ominus} \qquad (at)$$

Thus the introduction of a substituent A which facilitates electron transfer to a molecule can simultaneously lower the rate of bond cleavage since the negative charge no longer prefers this bond. Another reaction takes place instead of removal of the protecting group.

Utley et al. have demonstrated the cathodic cleavage of the methoxycarbonyl-activated *O*-benzyl protecting group[114]. An ESR study of the structure and kinetics of decomposition of radical anions in reactions (ae)–(ah) and (as) is reported in Ref. [115]. The rate constants for bond cleavage are decreased by introduction of the electron-acceptor substituent A. A quantum mechanical description of the effect is proposed in Ref. [116].

4.2. Use of Catalysts as Electron Carriers ("External Activation")

The role of an "inner activator" *i.e.* of an electron-acceptor substituent is first of all that it facilitates transfer of electrons to the system. The ensuing process may be regarded as a very fast (up to 10^{-12}—10^{-14} s) intramolecular transfer (redistribution) of charge, which provides the prerequisite high electron density on the R—XA bond prior to its cleavage.

In analogy to the above case (see Section 4.1) we investigated the feasibility of homogeneous electron transfer from an external activator A. This must have a high electron affinity for the substrate S but not form any chemical compound with it. Obviously the rate of charge transfer should decrease significantly, for it now depends on the difference of the standard potentials $\Delta E_0 = E_0^S - E_0^A$ of substrate S and activator A and its upper limit is diffusion controlled. If the bond cleavage is irreversible and both the electron transfer and the bond cleavage are fast compared to the competitive transformations of the radical anion $A^{\ominus\bullet}$, the reaction is both thermodynamically and kinetically favorable (cf. Refs. [1, 98]).

We carried out electro-deprotection of the substrate (S), *N*-(*p*-nitrobenzyloxycarbonyl)alanine *(25)*, using 4-nitrobiphenyl in the form of its radical anion $A^{\ominus\bullet}$ as activator. The transformation, which proceeds analogously to Eq. (af), was performed at $\Delta E_0 = -0.1$ V ($E_{1/2}^S = -1.14$ V, $E_{1/2}^A = -1.05$ V) in the absence of current and obtained the free amino acid in quantitative yield[1]. When the current was switched on (*i.e.* with continuous generation of $A^{\ominus\bullet}$) a catalytic current should appear similarly to that observed in the systems quinone/hydroquinone/H_2/Pd, nitro compound/camphor/$IO_4^{\ominus}$ *etc.* (see review given in Ref. [99]).

This phenomenon predicted by us in 1973[1], has in the meantime been confirmed by three groups of investigators working independently[100-102, 98, 67]; it evidently also occurred[98] in the experiments described by *Margel* and *Levy*[103][*].

$$A + e \rightleftharpoons A^{\ominus\bullet} \qquad \text{(au)}$$

$$A^{\ominus\bullet} + S \overset{k_3, K_3}{\rightleftharpoons} S^{\ominus\bullet} + A \qquad \text{(av)}$$

$$S^{\ominus\bullet} \overset{k_4, K_4}{\rightleftharpoons} P^{\ominus} + R^{\bullet} \qquad \text{(aw)}$$

$$A^{\ominus\bullet} + R^{\bullet} \overset{k_5, K_5}{\rightleftharpoons} R^{\ominus} + A \qquad \text{(ax)}$$

$$R^{\ominus} + DH \longrightarrow RH + D^{\ominus} \qquad \text{(ay)}$$

$$A^{\ominus\bullet} \xrightarrow{k_6} I \qquad \text{(az)}$$

The transformation of substrate S can be described by Equations (au)—(az)[1, 98, 100, 101].

A and $A^{\ominus\bullet}$ are, respectively, the electroneutral and radical anion forms of the activator, $P^{\ominus}$ and RH are products, DH is a proton donor (solvent, electrolyte, *etc.*), and I the product of a competitive deactivation of $A^{\ominus\bullet}$. When

$$\Delta E_0 = E_0^S - E_0^A = \frac{RT}{F} \ln K_3 < 0$$

the equilibrium constant K_3 is small, and the value K_4 (thermodynamic factor) must be high; besides the kinetic condition $k_3 > k_6$ must be fulfilled.

In principle the catalytic current allows determination of the rate constant of the rate-determining step—this is either the cleavage of the bond (k_4) or the electron transfer against the standard potential gradient (k_3). *Koutecky*'s solution[104], for which a convenient analytical function was recently developed[105], can be used to find k_3 (if k_3 is large, but very much smaller than k_4). *Britton* and *Fry* recently solved the problem in an analogous case (one irreversible step of type (av)+(aw), $k_3 \ll k_4$) using the method of chronoamperometry with stepwise change of potential[106]. We recently discussed the whole process (au)—(az) for arbitrary ratios of k_3 and k_4 and various values of K_3[107]. The solution for average polarographic currents was obtained with the help of a computer which provided plots of $(\bar{i}_k/\bar{i}_d) = F(k_3, k_4, K_3)$ ($\bar{i}_k$ = kinetic limiting current, $\bar{i}_d$ = diffusion current). We shall not go into an analysis of the individual results[107] here, but it must be noted that the solutions quoted previously[104, 105] are not suitable for the determination of k_3 and k_4 when these constants are of comparable order of magnitude.

Not only the cleavage of a bond [Eq. (aw)] can function as a fast irreversible step but also protonation, for instance in the activated hydrogenation of a difficultly reducible conjugated hydrocarbon S with the help of the easily reducible activator A [Eqs. (ba)—(bf)][98]:

$$A + e \rightleftharpoons A^{\ominus\bullet} \qquad \text{(ba)}$$

$$A^{\ominus\bullet} + S \rightleftharpoons S^{\ominus\bullet} + A \qquad \text{(bb)}$$

$$S^{\ominus\bullet} + DH \rightleftharpoons SH^{\bullet} + D^{\ominus} \qquad \text{(bc)}$$

$$A^{\ominus\bullet} + SH^{\bullet} \rightleftharpoons SH^{\ominus} + A \qquad \text{(bd)}$$

$$SH^{\ominus} + DH \longrightarrow SH_2 + D^{\ominus} \qquad \text{(be)}$$

$$A^{\ominus\bullet} + DH \longrightarrow I + D^{\ominus} \qquad \text{(bf)}$$

Several different aspects of such reactions have been discussed in the literature[98, 100-102].

Data on homogeneous catalytic electron transfer against the standard potential gradient for the removal of different protecting groups are listed in Table 1. Electro-deprotection is carried out at the reduction potentials of the activator; the required potential can be lowered (by more than 0.6 V) and the process essentially facilitated.

$$n\text{-}H_9C_4\text{–}O\text{–}CH_2\text{–}C_6H_5 + H_5C_6\text{–}C_6H_5 \xrightarrow[-2.65\ V]{2e,\,2\,[H^{\oplus}]} n\text{-}C_4H_9OH + H_3C\text{–}C_6H_5 + H_5C_6\text{–}C_6H_5 \qquad \text{(bg)}$$

The use of inner activation by introduction of a conjugated double bond was discussed in Section 4.1 for the removal of the *O*-benzyl protecting group. Table 1, No. 11, demonstrates the use of external activators for this purpose. The transformation [Eq. (bg)] proceeds according to first order kinetics and gives butanol and toluene in good yields (100% and 90% resp.)[67]. Thus one can succeed in carrying out electron transfer in a potential range lying beyond the discharge potential of the supporting electrolyte. Another example is illustrated in Fig. 2.

The possibility is revealed (see examples 6 and 7 in Table 1) of using the "chemical factor", *i.e.* the different stability of the radical anions $S^{\ominus\bullet}$ [that is the difference between constants k_4, Eq. (aw)] for the selective cleavage of protecting groups in addition to the electrochemical factor (the difference in reduction potentials). In fact, despite the higher half-wave potential (Table 2) the *N*-tosyl protecting group (−2.6 V) is

[*] It is possible that *Sease* and *Reed* considered an analogous process in 1970 (see reference to the author's report of *Reed*'s thesis in Ref. [100]). Unfortunately the works [101] and [102], were first accessible to us after contributions [98] and [67] had already been submitted for publication.

Table 1. Electron transfer reactions against potential gradient for the removal of protecting groups (in DMF, for conditions see original literature). $Z(NO_2)$ = *p*-nitrobenzyloxycarbonyl, Z = benzyloxycarbonyl, Tos = toluenesulfonyl, Bzl = benzyl.

Expt. No.	Protecting group	Substrate (S)	Activator (A)	ΔE_0 [V]	Product Yield [%]	Ref.
1	*N*-$Z(NO_2)$	$Z(NO_2)$-alanine	4-Nitrobiphenyl	−0.1	Alanine 100	[1]
2	*N*-Z	Z-glycine	Biphenyl	< −0.38	Glycine 100	[98]
3	*N*-Z	Z-butylamine [a]	Biphenyl	< −0.38	[b]	[98]
4	*O*-Tos	Ethyl toluenesulfonate	Anthracene	< −0.23	[b]	[101]
5	*N*-Tos	*N*,*N*-dimethyltoluenesulfonamide	Pyrene	< −0.33	[b]	[101]
6	*N*-Tos	*N*-*tert*-butyltoluenesulfonamide	Methyl benzoate	< −0.25	[b]	[98]
7	*N*-Tos	Tos-glycine	Methyl benzoate	< −0.32	Glycine 100	[98]
8	*N*-Tos	Tos-glycine	Stilbene	< −0.38	[b]	[98]
9	*N*-Tos	Tos-glycine	Anthracene	< −0.63	[b]	[98]
10	*O*-Bzl	Benzyl isopropyl ether	1-Methylnaphthalene	—	Toluene 93	[102]
11	*O*-Bzl	Benzyl butyl ether	Biphenyl	< −0.43	Butanol 100 Toluene 90	[67]

[a] Benzyl-*N*-butylcarbamate.
[b] Polarographic experiment.

Table 2. Removal of protecting groups by direct electroreduction (for details see text). The values quoted are the average half-wave potentials $E_{1/2}$ in V (*vs* SCE; in DMF, supporting electrolyte $(Alkyl)_4N^{\oplus}X^{\ominus}$). If no value is quoted either the protecting group is not suitable for the molecule to be protected or the possibility of the electroreduction has not been investigated.

Protecting group Y	Protected molecule R—NH—Y	R—O—Y	R—S—Y	R—CO—O—Y	$(RO)_2P(O)$—O—Y
Tosyl	2.6	2.2			
Tosyl	2.2 [a]	2.0 [a]			
Benzoyl	2.5	2.3			
Benzoyl	2.3 [a]				
Trityl	[b]	2.9	2.6	2.6	
Benzhydryl	[b]	3.0		2.6	
Benzyl	[b]	3.1	2.8	2.7	2.6
Phenyl	[b]	[b]	2.7	2.7	2.7
Cinnamyl	[c]	2.5		2.2	
Benzyloxycarbonyl	2.9	2.7	2.6		
Benzylidene		2.9			
o-Nitrophenylsulfenyl	1.1	1.0			
p-Nitrobenzyl		1.1		1.2	
p-Nitrobenzyloxycarbonyl	1.2	1.1			
2,2,2-Trichlorethoxycarbonyl	1.7 [d]	1.5 [d]	1.5 [d]		
2,2-Dichlorethoxycarbonyl	2.2 [d]				
2,2,2-Trichlorethoxy				1.7 [d]	
2,2-Dichlorethoxy				1.9 [d]	
2,2,2-Tribromethoxy				0.7 [d]	

[a] In methanol.
[b] No removal of protecting group up to the discharge potential of the supporting electrolyte.
[c] Reduction of molecule without removal of protecting group.
[d] In methanol. The given potential is that at which the electroreduction was carried out.

removed *earlier* in DMF than the *O*-benzoyl group (−2.3 V), since it is cleaved faster from the corresponding radical anion $S^{\ominus}$. It is interesting that *Horner* and *Singer* observed the same order in deprotection during electroreductions performed in methanol[33] (*N*-tosyl, $E_{1/2} = -2.2$ V; *N*-benzoyl, $E_{1/2} = -2.3$ V), but in this case the electrochemical factor was apparently determining [cf. Eq. (n)].

The directed modification of protecting groups and utilization of activators (electron carriers) permit variation of the potential at which electro-deprotection takes place. This opens new prospects for the use of electrochemical methods in preparative organic chemistry.

Different aspects of electron transfer reactions are touched upon in Refs. [117–119].

5. Conclusion

A great number of protecting groups (see Table 2) can be removed by electrolysis. The essential advantages of the method are:

a) mild conditions in the electrochemical cleavage;
b) high degree of selectivity; the required potential can be shifted into a favorable range by "inner" or "external" activation;
c) uniform experimental technique in contrast to chemical methods, *i.e.* the technique is the same for all protecting groups to be removed. It permits removal of several different protecting groups at one and the same time during the last stage of the synthesis (compare Section 3.4) and furnishes the prerequisites for working out standard methods.

The range of potential for removal of various protecting groups extends from *ca.* −1 to *ca.* −3 V (*vs* SCE). A general regularity may be noted—the removal of one and the same protecting group (Y) is facilitated along the series N—Y < O—Y < S—Y < C(O)O—Y, *i.e.* according to increasing nucleophilicity of the blocking group. By "external activation" the potential of deprotection may be essentially decreased (by at least 0.5—0.7 V) compared to the potentials listed in Table 2.

The protecting groups listed in Table 2 are universal. An example of a special protecting group is the nitro group sug-

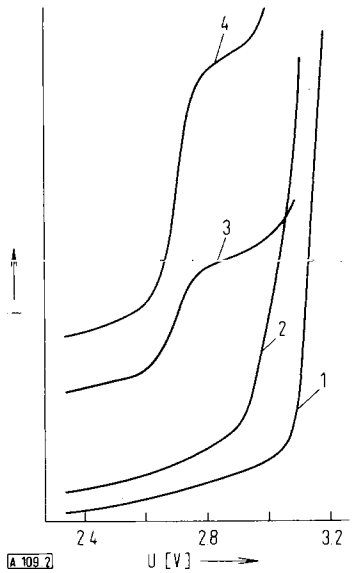


Fig. 2. Catalytic polarographic current in a system with electron transfer against potential gradient beyond the supporting electrolyte discharge range. 1: 0.04 M $(C_4H_9)_4N^{\oplus}ClO_4^{\ominus}$ in DMF; 2: 1.6×10^{-3} M benzyl-*N*-butylcarbamate (*N*-benzyloxycarbonyl-*n*-butylamine) (S); 3: 4.1×10^{-4} M biphenyl (A); 4: mixture of A and S (schematic); see Table 1, No. 3. Potentials referred to SCE.

gested here for blocking the guanidine residue of arginine[108] and which can likewise be removed by electroreduction[109]. The possibility of using not only cathodic but also anodic reactions for the removal of protecting groups can so far be illustrated by only a few examples: The electrooxidative cleavage of benzyl and benzhydryl ethers[110].

$$H_5C_6{-}CH_2{-}O{-}C_8H_{17} \xrightarrow[-2e,\,-2\,H^{\oplus},\,+H_2O]{Pt,\,CH_3CN} H_{17}C_8OH + H_5C_6{-}CHO \qquad \text{(bh)}$$

$$(H_5C_6)_2CH{-}O{-}C_{12}H_{25} \xrightarrow[-2\,e,\,-2\,H^{\oplus},\,+H_2O]{Pt,\,CH_3CN} H_{25}C_{12}OH + (C_6H_5)_2CO \qquad \text{(bi)}$$

The yields of free alcohols are 60—70 %.

Weinreb et al. have discussed the anodic cleavage of the benzyl protecting group[120].

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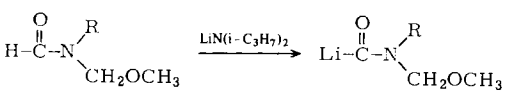
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying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

α-Hydroxycarboxamides from *N,N*-Bis(methoxymethyl)carbamoyllithium and Carbonyl Compounds

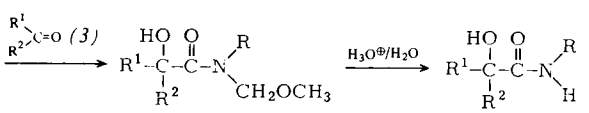
By *Ulrich Schöllkopf* and *Heiko Beckhaus*[*]

α-Hydroxycarboxamides of type *(6)* are versatile intermediates in preparative chemistry. Hitherto, the method used for their synthesis from carbonyl compounds *(3)* involved initial conversion of the latter to cyanohydrins; this method, however, failed in many cases owing to the instability of the cyanohydrin. We have now found an alternative method which also permits synthesis of the *N*-alkyl derivatives *(7)*.

When the *N*-methoxymethylformamides *(1a)* and *(1b)* protected at the amino group[1] are used as starting material, reaction with lithium diisopropylamide affords the *N*-methoxymethylcarbamoyl derivatives *(2a)* and *(2b)*, which are converted *in situ* with the carbonyl compound *(3)* into the *N*-substituted α-hydroxycarboxamides *(4)* and *(5)*, respectively[2]. Compounds *(4)* and *(5)* can be readily converted into the carboxamides *(6)* and *(7)*, respectively, by acid hydrolysis[1].



(1a), R = CH_2OCH_3 *(2a)*, R = CH_2OCH_3
(1b), R = CH_3 *(2b)*, R = CH_3



(4), R = CH_2OCH_3 *(6)*, R = H
(5), R = CH_3 *(7)*, R = CH_3

	R^1	R^2	*(4)* Yield [%]	*(4)* B.p. [°C/torr] M.p. [°C]	*(5)* Yield [%]	*(5)* B.p. [°C/torr] M.p. [°C]
a	H	C_6H_5	74	142—143/0.05	76	49
b	—$(CH_2)_5$—		44	119/0.01	39	107/0.01
c	C_6H_5	C_6H_5	88	85—86	85	110—112
d	H	C_6H_5—CH=CH	—	—	40	62—63

N,N-Bis(methoxymethyl)formamide (1a)

A solution of freshly distilled formamide (22.5 g, 0.5 mol) in tetrahydrofuran (50 ml) is added dropwise to a stirred suspension of sodium hydride (24 g, 1 mol) in tetrahydrofuran (400 ml) such that the temperature of the reaction mixture never exceeds 30 °C. After 10 minutes' stirring at room temperature chloromethyl methyl ether (80.5 g, 1 mol) is added dropwise (also at room temperature) over a period of 30 min to the mixture, which is then stirred for a further 12 hours, filtered (under nitrogen), and the solvent removed by distillation in a rotary evaporator at 14 torr (bath temperature 50 °C). 43.3 g (65% yield) of *(1a)* (b.p. 58—59 °C/0.1 torr; 20 cm-Vigreux column) is obtained. The product is sometimes contaminated with a little formaldehyde. ^{1}H-NMR (CCl_4): τ = 1.72 (s, CHO), 5.33 (d, N—CH_2—O, coalescence temperature 130 °C), 6.78 (s, CH_3).—*(1b)* was prepared in the same way as *(1a)* with the exception that 59 g (1 mol) of *N*-methylformamide was used; yield 80.5 g (78 %), b.p. 73—75 °C/15 torr.

N,N-Bis(methoxymethyl)-1-hydroxycyclohexanecarboxamide (4b)

A solution of lithium diisopropylamide (40 mmol) [prepared from 1.6 N butyllithium (25 ml) and diisopropylamine (4.04 g) in tetrahydrofuran (40 ml) at 0 °C] previously cooled to −60 °C is added dropwise at −75 °C over a period of 20 min to a stirred solution of *(1a)* (5.3 g, 40 mmol) and cyclohexanone (3.93 g, 40 mmol) in tetrahydrofuran (100 ml). After 3 h the mixture is allowed to warm to room temperature, poured into 200 ml of saturated ammonium chloride solution, and the organic phase separated off and dried over sodium sulfate. The dried solution is then distilled in a rotary evaporator at 14 torr (bath temperature 60 °C). The residue of crude *(4b)* is purified chromatographically on *ca.* 500 g silica gel (Merck; 0.2—0.5 mm) with ether as eluent. 4.1 g (44 %) of *(4b)* is obtained. ^{1}H-NMR ($CDCl_3$): τ = 5.05 (s, N—CH_2—O), 6.37 (s, OH replaceable by D with D_2O, 6.7 (s, O—CH_3), 8.0—8.8 (m, —CH_2—).

N-Methylmandelic acid amide (7a) from (5a)

Concentrated hydrochloric acid (1 g) is added dropwise to a solution of *(5a)* (3 g) in ethanol (50 ml). After 12 hours' stirring at room temperature the reaction solution is concentrated in a rotary evaporator (bath temperature 60 °C); the residue is taken up in ether and washed with sodium bicarbonate solution. The washed ethereal phase is finally worked up in the usual way *(vida supra)*. *(7a)* (m.p. 97—98 °C) is obtained in 92 % yield (2.18 g).

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CAS Registry numbers:
(1a), 57675-06-6; *(1b)*, 5129-79-3; *(2a)*, 57675-07-7; *(2b)*, 57675-08-8; *(3)*, R^1 = H, R^2 = C_6H_5, 100-52-7; *(3)*, R^1R^2 = —$(CH_2)_5$—, 108-94-1; *(3)*, R^1 = R^2 = C_6H_5, 119-61-9; *(3)*, R^1 = H, R^2 = C_6H_5—CH=CH, 104-55-2; *(7a)*, 2019-72-9

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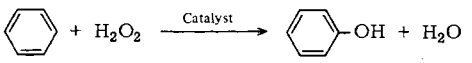
[1] The methoxymethyl protecting group is stable toward alkalis and unstable toward acids.

[2] For technique cf. *B. Banhidai* and *U. Schöllkopf*, Angew. Chem. *85*, 861 (1973); Angew. Chem. Int. Ed. Engl. *12*, 836 (1973); *R. R. Fraser* and *P. R. Hubert*, Can. J. Chem. *52*, 185 (1974).

Continuous Electrocatalytic Synthesis of Phenol from Benzene and Hydrogen Peroxide[1]

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

Despite the well established methods of synthesizing phenol there has long been interest in the realization of a practicable synthesis of phenol from benzene and hydrogen peroxide.



All previous results however have been unsatisfactory, since the reaction usually affords only poor yields and is not very selective. This applies also for the reaction with iron(II) as catalyst[2]. Under the usual reaction conditions mixtures of phenol, hydroquinone, pyrocatechol, as well as higher oxidation products and biphenyl are formed; the yields of phenol are less than 10% based on consumed hydrogen peroxide[2, 3]. Recent analytical investigations[4], on the other hand, show that phenol formation is preferred if the following conditions are maintained: a large excess of benzene and iron(III) or copper(II) salts, a hydrogen peroxide concentration not greatly exceeding the concentration of iron(II), pH *ca.* 1, *T* *ca.* 25 °C.

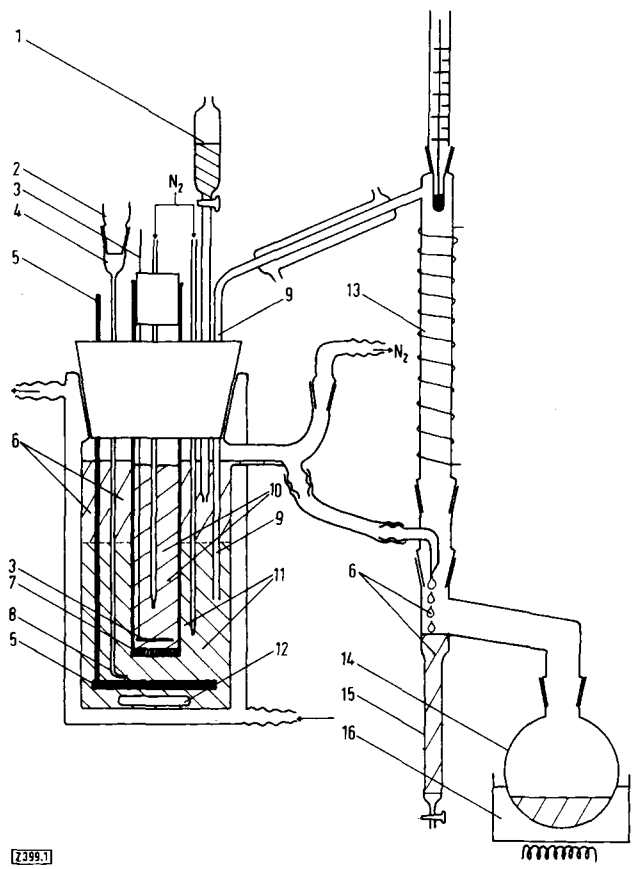


Fig. 1. Glass cell for electrolytic synthesis of phenol. 1, dropping funnel with 30% H_2O_2; 2, reference electrode; 3, anode (platinum); 4, salt bridge; 5, cathode (graphite); 6, benzene phase enriched with phenol; 7, glass cylinder with frit as anode compartment; 8, luggin capillary; 9, benzene inlet tube; 10, anolyte; 11, catholyte: aqueous phase with suspended benzene; 12, magnetic stirrer; 13, heated column for distillation of benzene; 14, receiver for enriched benzene/phenol mixture; 15, water separator; 16, thermostatic heating bath.

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These optimum conditions must be maintained throughout the whole duration of the reaction. This can be achieved with the "electrocatalytic" method, for it permits maintenance of a constant iron(II) concentration by continuous replenishment of the iron(II) consumed in side-reactions at the electrode. The ratio of iron(II) to iron(III) and copper(II) thus remains unchanged. Furthermore, the consumption and replacement of hydrogen peroxide can be controlled by monitoring the cathodic working potential. Of great importance is the continuous extraction of oxidation-labile phenol[5] and other organic products from the aqueous catalyst phase into the supernatant benzene. The two-phase system also allows continuous operation since the benzene can be recycled and readily separated from the products.

Procedure

A solution of iron(III) sulfate (3.5 mmol), copper(II) sulfate (7 mmol), and 60% perchloric acid (1.17 g) in water (70 ml) was transferred to the cathode compartment of a glass cell (beaker) (see Fig. 1) and covered with a layer of benzene. The anode compartment contained an aqueous solution 0.1 M w.r.t. perchloric acid and 0.2 M w.r.t. sodium perchlorate. After preliminary electrolytic generation of 2 mmol iron(II) a constant current of 50 mA was maintained and 30% hydrogen peroxide was added dropwise with stirring and passage of nitrogen at 25 °C whenever the working potential of the cathode reached its original value. The overflow of phenol-enriched benzene was continuously distilled and the benzene recycled into the reaction vessel. After addition of 20.4 mmol H_2O_2 and consumption of 7 mF, the products were determined quantitatively on a Tenax column against tetradecane as internal standard. 13.0 mmol of phenol and 0.1 mmol of biphenyl were obtained, *i.e.* 64% and 0.24%, respectively, based on H_2O_2.

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Phenol, 108-95-2; benzene, 71-43-2; hydrogen peroxide, 7722-84-1; biphenyl, 92-52-4

[1] Part 1 of Indirect Electrochemical Processes. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.
[2] *C. F. Cross, E. J. Bevan,* and *Th. Heiberg,* Chem. Ber. *33*, 2015 (1900).
[3] *J. R. L. Smith* and *R. O. C. Norman,* J. Chem. Soc. *1963*, 2897.
[4] *Ch. Walling* and *R. A. Johnson,* J. Am. Chem. Soc. *97*, 363 (1975); *Ch. Walling,* Acc. Chem. Res. *8*, 125 (1975).
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Synthesis of α,β-Dehydro Amino Acid Esters and *N*-*tert*-Butoxycarbonyl α,β-Dehydro Amino Acids[**]

By *Hans Poisel* and *Ulrich Schmidt*[*]

α,β-Dehydro amino acids have been claiming increasing attention in the past few years as components of antibiotic peptides and intermediates in biosyntheses[2]. We recently described the transformation of amino acids into *N*-acyl dehydro amino acid esters and amides by *N*-chlorination and dehydrochlorination[3]. By using *N*-*tert*-butoxycarbonyl amino (Boc-amino) acid derivatives as starting compounds this reaction sequence can also be employed for the synthesis of the *free* dehydroamino acid esters and Boc-dehydro amino

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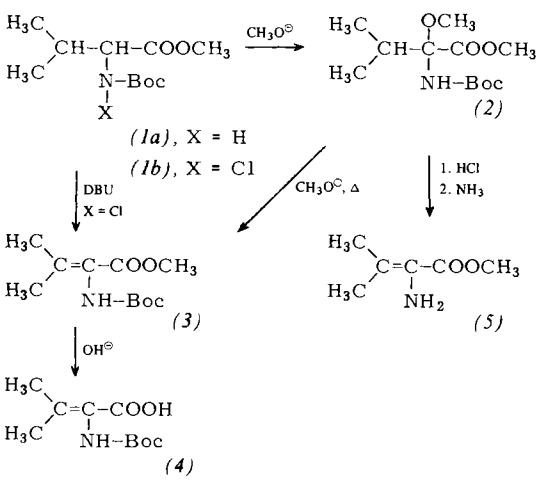
[**] Amino Acids and Peptides, Part 19.—Part 18: ref. [1].—Also: Dehydro Amino Acids, Part 6.—Part 5: ref. [1].

acids, which are of importance for the synthesis of dehydropeptides.

The method is demonstrated for the case of Boc-valine methyl ester *(1a)*: *N*-chlorination [to *(1b)*] and reaction with methoxide to achieve subsequent dehydrochlorination and addition of methanol, without isolation of intermediates, affords good yields of the Boc-α-methoxy amino acid ester *(2)*, which on reaction with hydrogen chloride in ether suffers loss of the *tert*-butoxycarbonyl group and methanol with formation of dehydrovaline ester hydrochloride. The free amino acid ester *(5)*[4] is easily accessible from the hydrochloride by reaction with ammonia. This reaction sequence can also be extended to the preparation of dehydrophenylalanine ester and dehydroleucine ester[5]. The NMR spectrum of the latter also shows signals of the tautomeric imino acid ester; the dehydrophenylalanine ester and dehydrovaline ester *(5)*, on the other hand, are present exclusively as enamines.



Base-catalyzed elimination of methanol from the methoxy compound *(2)* yields the Boc-dehydrovaline ester *(3)* which can be hydrolyzed to Boc-dehydrovaline *(4)*. More favorable, and especially more suited for the synthesis of Boc-dehydroaminobutyric acid, however, is the dehydrochlorination of the corresponding *N*-chloro compound *(1b)* with diazabicycloundecene (DBU) and hydrolysis of the resulting Boc-dehydro amino acid ester *(3)*. Dehydroaminobutyric acid has been found to be present in various antibiotic peptides (nisin, subtilin[6]).

α,β-Dehydrovaline methyl ester (5)

A solution of sodium (1.30 g, 56.5 mmol) in methanol (100 ml) is slowly added dropwise to an ice-cooled solution of *(1a)* (9.24 g, 40.0 mmol) and *tert*-butyl hypochlorite (6.0 g, 55.6 mmol) in anhydrous ether (200 ml). When the addition is complete, the ice-bath is removed and the mixture stirred for 1 h. The solvent is then removed by distillation *in vacuo* and the residue taken up in dichloromethane and shaken with 0.01 N HCl followed by a saturated $NaHCO_3$ solution. After removal of the dichloromethane the residue is distilled in a bulb-tube under high vacuum (bath temp. 120°C). 9.8 g (94 %) of *(2)* is obtained as colorless crystals, m.p. 52—55°C (petroleum ether); ^{1}H-NMR ($CDCl_3$): δ = 0.92 (d, 3H); 1.00 (d, 3H); 1.48 (s, 9H); 2.22—2.70 (m, 1H); 3.34 (s, 3H); 3.80 (s, 3H); 5.48 (br. s, 1H).

An ice-cooled solution of *(2)* (3.0 g) in anhydrous ether (50 ml) is saturated with dry HCl. The solution is allowed to stand overnight and then evaporated to dryness under vacuum. The crystalline residue [*ca.* 1.9 g *(5)*·HCl] is treated several times with anhydrous ether and dried under vacuum. To liberate *(5)*, 1.8 g of the hydrochloride is dissolved in 15 ml dichloromethane, and the ice-cooled solution saturated with dry ammonia; the ammonium chloride formed is removed by filtration and the filtrate concentrated by evaporation *in vacuo*. The oily residue is distilled in a bulb-tube. 1.2 g (86 %) of *(5)*, b.p. 76°C/11 torr is obtained; ^{1}H-NMR ($CDCl_3$): δ = 1.76 (s, 3H); 2.06 (s, 3H); 3.24 (br. s, 2H); 3.76 (s, 3H).

Methyl N-tert-butoxycarbonyl-α,β-dehydro-α-aminobutyrate

Methyl Boc-α-aminobutyrate (1.76 g, 8.1 mmol) is dissolved in anhydrous ether (40 ml). The ice-cooled solution is treated first with *tert*-butyl hypochlorite (1.40 g, 13.0 mmol) and then dropwise with 1 ml of a 1 % solution of Na in methanol. After 15 min the reaction mixture is examined by thin-layer chromatography (silica gel plates, chloroform). If any starting material is found, the mixture is treated with a further 0.70 g *tert*-butyl hypochlorite and 0.50 ml of the methoxide solution. The reaction solution is concentrated *in vacuo*, the residue taken up in chloroform, washed twice with a small volume of water, and dried. After removal of chloroform by evaporation, 1.95 g (96 %) of the oily *N*-chloro product [of type *(1b)*] is obtained; ^{1}H-NMR ($CDCl_3$): δ = 1.0 (t, 3H); 1.51 (s, 9H); 1.60—2.22 (m, 2H); 3.76 (s, 3H); 4.6—4.82 (m, 1H).

1.90 g (7.6 mmol) of the crude oil is dissolved in ether (50 ml) and, after addition of 1.15 g (7.6 mmol) of diazabicycloundecene (DBU), is heated to boiling. When no more *N*-chloro compound is present on examination by thin-layer chromatography (2—3 h), DBU·HCl is separated off by filtration, the ether replaced by chloroform, and the resulting solution washed first with dil. HCl and then a saturated solution of $NaHCO_3$. After drying and removal of solvent the residue is distilled under high vacuum in a bulb-tube (bath temp. 120°C). The oily product of type *(3)* (1.15 g, 75 %) crystallizes on being rubbed with petroleum ether; m.p. 70—72°C; ^{1}H-NMR ($CDCl_3$): δ = 1.48 (s, 9H); 1.80 (d, 3H); 3.78 (s, 3H); 6.20 (br. s, 1H); 6.66 (q, 1H).

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(1a), 58561-04-9; *(1b)*, 58561-05-0; *(2)*, 58561-06-1; *(3)*, 55478-14-3; *(4)*, 58561-07-2; *(5)*, 10409-27-5; *(5)*·HCl, 53267-36-0; *tert*-butyl hypochlorite, 507-40-4; methyl *N-tert*-butoxycarbonyl-α,β-dehydro-α-aminobutyrate, 55477-81-1; methyl Boc-α-aminobutyrate, 58561-08-3

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A Simple Synthesis of Cyclopentadienylboranes[**]

By *Peter Jutzi* and *Arnulf Seufert*[*]

Because of their reactive silicon-carbon bond cyclopentadienylsilanes have proved to be preparatively valuable agents

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Table 1. Physical Data of compounds *(1)*—*(10)*. The isomers *(2)*/*(4)* and *(3)*/*(5)* could not previously be separated.

Compd.	B.p. [°C/torr] M.p. [°C]	Yield [%]	Reaction temp. [°C]	^{11}B-NMR [a]	^{1}H-NMR [b]
(1)	35/10	10	−45	−48.9	H-2: −7.63 m; H-3, H-4: −6.65 m [2H]; H-5: −3.3 m [2H]; CH_3: −2.30 m, −2.15 m [3H]
(2), *(4)*	53/0.5	85	60	−50.2	*(2)*: H-2 to H-5: −6.42 br. m [4H]; $Si(CH_3)_3$: +0.06 s [9H]; *(4)*: H-2: −7.78 m, −7.83 m; H-3, H-4: −7.06 m, −6.95 m [2H]; H-5: −3.52 m, −3.39 m [2H]; $Si(CH_3)_3$: −0.38 s [9H]
(3), *(5)*	64/0.3	8	0	−51.1	*(3)*: H-2 to H-5: −6.45 br. [4H]; $Si(CH_3)_3$: −0.28 s [9H]; *(5)*: H-2: −7.85 [1H]; H-3, H-4: −7.02 m [1H]; H-5: −3.59 m [2H]; $Si(CH_3)_3$: −0.48 s [9H]
(6)	75/0.5	65	60	−49.2	H-2: −7.65 m [1H]; H-3, H-4: −7.22 to −6.45 m [2H]; $Si(CH_3)_3$: −0.32 s [18H]
(7)	102/0.6	75	0	−50.1	H-2: −7.68 m [1H]; H-3, H-4: −7.18 to −6.25 m [2H]; $Si(CH_3)_3$: −0.20 s [18H]
(8)	66/0.5	51	80	−50.8	H-2, H-3: −7.64 t [2H]; H-5: −3.63 t [2H]; $J_{2,5}$: 1.7 Hz
(9)	85 (dec.)	52	−30	−51.7	H-2, H-3: −7.60 t [2H]; H-5: −3.77 t [2H]; $J_{2,5}$: 1.7 Hz
(10)	125 (dec.)	48	0	−36.8	H-2, H-3: −7.80 t [2H]; H-5: −3.95 t [2H]; $J_{2,5}$: 1.7 Hz

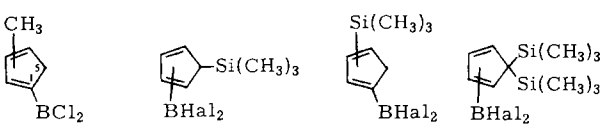
[a] δ [ppm] against $BF_3 \cdot O(C_2H_5)_2$ external.
[b] δ [ppm] against TMS internal.

for the transfer of cyclopentadienyl ligands to other elements under mild conditions[1, 2]. We report here on the use of this synthetic principle for the preparation of cyclopentadienylboranes; the extremely few compounds of this type so far reported were prepared by comparatively complicated methods[3].

Reaction of trimethylsilyl-substituted cyclopentadienes[4, 5] with boron trihalides leads *via* cleavage of trimethylhalosilane to formation of the corresponding dihaloboryl-substituted cyclopentadienes:

$$R\text{—}CpSi(CH_3)_3 + BHal_3 \rightarrow R\text{—}CpBHal_2 + (CH_3)_3SiHal$$

To demonstrate the preparative scope of this method we have so far synthesized the compounds *(1)*—*(7)*; they are colorless liquids and extremely sensitive to air.

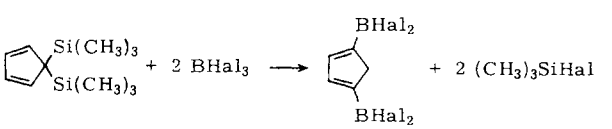


(1) *(2), (3)* *(4), (5)* *(6), (7)*

Hal = Cl in *(2)*, *(4)*, *(6)*; Hal = Br in *(3)*, *(5)*, *(7)*

In most cases the reactions proceed almost quantitatively under very mild conditions. A loss in yield only occurs during distillative workup of some compounds due to their thermolability.

Polyborinated cyclopentadienes could not be prepared by the previously known methods for the synthesis of monoborylcyclopentadienes, since the B—C bond is cleaved on attempted metalation[3a, 6]. With the present method, however, diborylcyclopentadienes can also be very easily synthesized. Thus, on reaction of 5,5-bis(trimethylsilyl)cyclopentadiene with 2 equivalents of boron trihalide the crystalline compounds *(8)*, *(9)*, and *(10)*, which are very sensitive to air, are formed.



Hal = Cl in *(8)*, Br in *(9)*, I in *(10)* *(8), (9), (10)*

The structures of compounds *(1)*—*(10)* were confirmed by analytical as well as mass spectrometric and NMR spectroscopic data (see Table 1). The dihaloboryl group and the methyl group are always bound to a vinylic C atom of the cyclopentadiene system. The trimethylsilyl ligand is usually fixed to an allylic C atom and is thus responsible for the fluctional structure ([1,5] sigmatropic rearrangement) of the compounds *(2)*, *(3)*, *(6)*, and *(7)*. No dynamic behavior is exhibited by compounds *(1)*, *(4)*, *(5)*, *(8)*, *(9)*, and *(10)* at room temperature.

Experimental:

Compounds *(1)*—*(8)*: The respective reactants are stirred together for 2 h at the temperatures quoted in Table 1. The products *(1)*—*(8)* are isolated from the reaction solution by fractional distillation.

Compounds *(9)* and *(10)*: To a solution of 5,5-bis(trimethylsilyl)cyclopentadiene in pentane are added concentrated pentane-solutions of BBr_3 and BI_3 respectively; the additions are carried out slowly and with stirring at the temperatures given in Table 1. The precipitated crystals are filtered off and recrystallized from methylcyclohexane [*(9)*] and dichloromethane/pentane (2:1) [*(10)*], respectively.

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(1), 58581-25-2; *(2)*, 58581-26-3; *(3)*, 58581-27-4; *(4)*, 58581-28-5; *(5)*, 58581-29-6; *(6)*, 58581-30-9; *(7)*, 58581-31-0; *(8)*, 58581-34-3; *(9)*, 58581-35-4; *(10)*, 58581-36-5; 5,5-bis(trimethylsilyl)cyclopentadiene, 33630-76-1; BCl_3, 10294-34-5; BBr_3, 10294-33-4; BI_3, 13517-10-7

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Low-Temperature X-Ray Structure Analysis of 1-Benzothiepin

By *Noritake Yasuoka, Yasushi Kai, Nobutami Kasai, Toshio Tatsuoka*, and *Ichiro Murata*[*]

Structural data of the thiepin ring have hitherto been unavailable because of its thermal instability; on the other hand, its stable dioxide derivatives have been fully investigated[1, 2]. Here we wish to report the molecular structure of 1-benzothiepin at low temperature (−140 °C).

1-Benzothiepin *(1)* (for synthesis, see Ref. [3]) was chromatographed on alumina (deactivated with 5% water, hexane, −20 °C) and subsequently recrystallized from hexane at −60 °C. The resulting pale yellow platelets, m.p. 23.5—24.5 °C, were examined on a Rigaku automated single crystal diffractometer with $Mo_{K\alpha}$ radiation; the low temperature being attained by the gas-flow technique with liquid nitrogen.

Compound *(1)* is monoclinic, $a=12.403(9)$, $b=6.187(3)$, $c=10.856(5)$ Å, $\beta=107.45(4)°$, space group $P2_1/n$ (No. 14), $d_{calc.}=1.34\,g\,cm^{-3}$ for $Z=4$.

The structure was solved by the direct method with the MULTAN program. At the earlier stage of the refinement, the larger values of isotropic temperature factors observed in the thiepin ring than the benzo ring indicated the presence of disorders. According to difference Fourier syntheses a minor contribution (15%) of a mirror image form of the molecule is plausible. This partially disordered model of the structure could be refined successfully including hydrogen atoms (with isotropic temperature factors) to a final R value of 0.069 (1586 observed reflections).

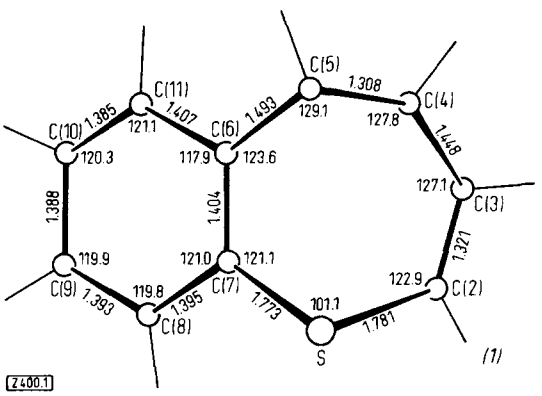

Fig. 1. Bond lengths and angles in 1-benzothiepin *(1)*. Maximum errors ±0.005 Å and ±0.3°, respectively.

The molecular structure projected onto the plane passing through C(2), C(3), C(6), and C(7) is shown in Figure 1 with bond lengths and angles. It is remarkable that the molecular geometry is quite similar to that of 1-benzothiepin 1,1-dioxide already reported by the present authors[2]. The thiepin ring is in a boat conformation with angles of 49.1 and 30.0° between the base plane and the "bow" [C(2)—S—C(7)] and "stern" [C(3)—C(4)—C(5)—C(6)] planes, respectively.

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CAS Registry numbers:
(1), 264-82-4; 1-benzothiepin 1,1-dioxide, 41887-86-9

[1] *H. L. Ammon, P. H. Watts*, and *J. M. Stewart*, Acta Crystallogr. *B 26*, 1079 (1970).
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Total Synthesis of Methionine-Enkephalin

By *Wolfgang Voelter, Claus Bürvenich, Hans Horn, Hubert Kalbacher*, and *Emanuel Pietrzik*[*]

On the 18th of December 1975, *Hughes et al.*[1] reported the identification of two pentapeptides isolated from pig brains: in the vas deferens of the mouse, methionine-enkephalin (H-Tyr-Gly-Gly-Phe-Met-OH) was found to be twenty times more active, and leucine-enkephalin (H-Tyr-Gly-Gly-Phe-Leu-OH) ten times more active compared to normorphine. We now present a preliminary report of a classical total synthesis of the "endogenous opiate" methionine-enkephalin[2].

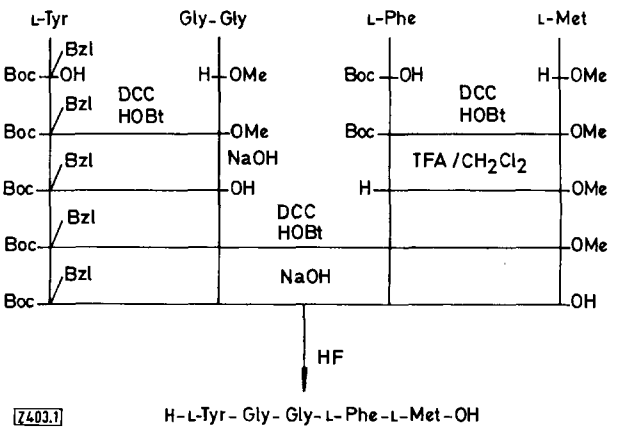

Fig. 1. Synthetic strategy for the preparation of methionine-enkephalin.

The synthetic strategy is shown in Figure 1. The following starting materials were synthesized for the preparation of the peptide: Boc-L-Tyr(Bzl)-OH[3] (m.p. 109 °C; $[\alpha]_D=+5°$, $c=1$, CH_3COOH), H-Gly-Gly-OMe·HCl[4] (prepared from H-Gly-Gly-OH and thionyl chloride/CH_3OH (1.2:12), m.p. 122 °C), Boc-L-Phe-OH[3] (m.p. 83—84 °C, $[\alpha]_D=-4°$, $c=1$, CH_3COOH), and H-L-Met-O-Me·HCl[4] (m.p. 144 °C; $[\alpha]_D=+26.3°$, $c=1$, H_2O).

Twelve hours' coupling of Boc-L-Tyr(Bzl)-OH (1.02 g, 2.75 mmol) and H-Gly-Gly-OMe·HCl (0.50 g, 2.75 mmol) with dicyclohexylcarbodiimide (DCC) (0.6 g, 2.90 mmol) and 1-hydroxybenzotriazole (HOBt) (0.37 g, 2.75 mmol) in DMF affords Boc-L-Tyr(Bzl)-Gly-Gly-OMe which is hydrolyzed at pH 12.5 (adjusted with 1 N NaOH) in dioxane/water (1:1) (yield 1.0 g = 75 %).

The protected C-terminal peptide fragment H-L-Phe-L-Met-OMe is obtained *via* Boc-L-Phe-L-Met-OMe by reaction of Boc-L-Phe-OH (5.3 g, 20 mmol) and H-L-Met-OMe·HCl (3.99 g, 20 mmol) with DCC (4.12 g, 20 mmol) and HOBt (5.4 g, 40 mmol) in DMF; the *tert*-butyloxycarbonyl protecting group

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is removed with trifluoroacetic acid (TFA/CH_2Cl_2, 1:1; yield 5.9 g = 70 % as TFA derivative).

In analogy to the above two peptide linkages the protected pentapeptide Boc-L-Tyr(Bzl)-Gly-Gly-L-Phe-L-Met-OMe (1.2 g, 77 % yield) was obtained from Boc-L-Tyr(Bzl)-Gly-Gly-OH (1 g, 2 mmol) and H-L-Phe-L-Met-OMe·CF_3COOH (0.85 g, 2 mmol). Twelve hours' hydrolysis of the methyl ester at room temperature in methanol/water (1:1) at pH 12.5 (adjusted with 1 N NaOH), neutralization with 1 N HCl, and evaporation was followed by removal of the remaining protecting group with HF in the presence of anisole, and precipitation of the peptide with ether. An aqueous solution of the peptide was then stirred for 90 min with Dowex 1×8 (OH form). After the resin had been filtered off the peptide was recrystallized from ether/alcohol mixtures (yield 540 mg = 61 %): The purity was established by thin layer chromatography (silica gel plates (F_{254}) from Merck, mobile phase: *n*-butanol/glacial acetic acid/water (3:1:1), $R_f = 0.42$).

Methionine-enkephalin melts and decomposes at 195 °C; its rotatory power $[\alpha]_D^{25}$ is +31.5° ($c = 0.96$, MeOH).

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CAS Registry numbers:
Boc-L-Tyr(Bzl)-OH, 54784-43-9; H-Gly-Gly-OMe·HCl, 2776-60-5; H-Gly-Gly-OH, 556-50-3; Boc-L-Phe-OH, 13734-34-4; H-L-Met-O-Me·HCl, 2491-18-1; Boc-L-Tyr(Bzl)-Gly-Gly-OMe, 57729-52-9; H-L-Phe-L-Met-OMe, 22248-60-8; Boc-L-Phe-OH, 13734-34-4; Boc-L-Phe-L-Met-OMe, 40290-63-9; Boc-L-Tyr-(Bzl)-Gly-Gly-L-Phe-L-Met-OMe, 58569-54-3; H-L-Tyr-Gly-Gly-L-Phe-L-Met-OH, 58569-55-4

[1] *J. Hughes, T. W. Smith, H. W. Kosterlitz, L. A. Fothergill, B. A. Morgan,* and *H. R. Morris,* Nature *258*, 577 (1975).
[2] *D. Gupta* and *W. Voelter:* Hypothalamic Hormones, Structure, Synthesis and Biological Activity. Verlag Chemie, Weinheim 1975.
[3] *E. Schnabel,* Justus Liebigs Ann. Chem. *702*, 188 (1967).
[4] *M. Brenner* and *W. Huber,* Helv. Chim. Acta *36*, 1109 (1953).

Oxidation of Alkylidenetriphenylphosphoranes with Phosphite-Ozone Adducts

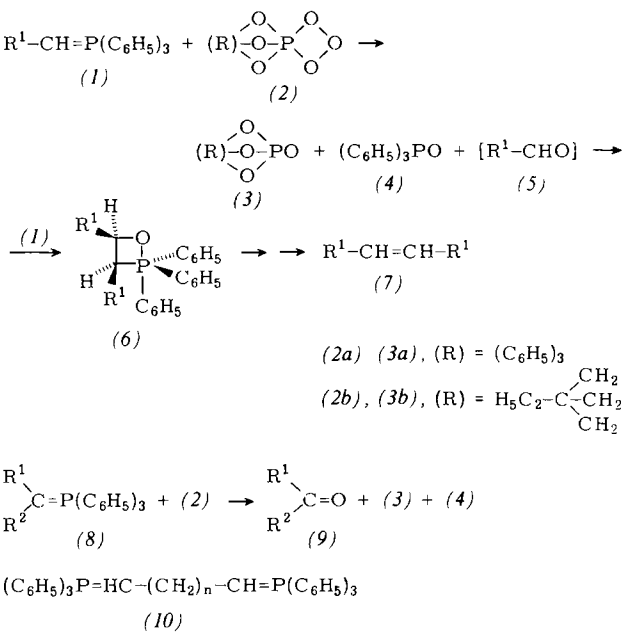
By *Hans Jürgen Bestmann, Lothar Kisielowski,* and *Werner Distler*[*]

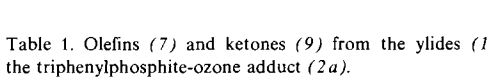
Alkylidenetriphenylphosphoranes *(1)* and *(8)* are oxidized by phosphite-ozone adducts[1] such as *(2a)* and *(2b)*. Ylides of the general structure *(1)* afford olefins *(7)*, phosphates *(3)*, and triphenylphosphane oxide *(4)*, while those of type *(8)*, R^1, $R^2 \neq H$, give ketones *(9)*. The reaction of *(1)* with *(2)* presumably proceeds *via* aldehydes *(5)* (Table 1).

Bifunctional ylides *(10)*, $n > 4$, react with *(2)* to form macrocyclic polyolefins; thus the bis(alkylidenetriphenylphosphorane) *(10)*, $n = 8$, accessible from 1,10-bromodecane furnishes a mixture of 20-, 30-, 40-, 50-, and 60-membered rings having two to six double bonds[2].

The preparative advantages of the new method of oxidation compared with autoxidation[3] lie (a) in accurate dosing of the oxidizing agent, (b) in the considerably milder reaction conditions (reaction temperature −75 °C), (c) in the possibility of converting stable ylides which are not attacked by oxygen into 1,4-diacylethylenes or 1,2-diketones, and (d) in the higher yields; thus the ylide derived from axerophthene gives a 75 % yield of β-carotene on treatment with *(2a)*[4].

In contrast to other oxidations with *(2)*[1b,1c] the oxygen is not transferred from *(2)* to *(1)* or *(8)* in the form of





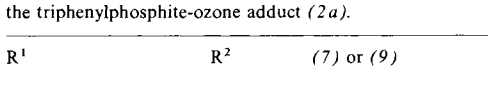


Table 1. Olefins *(7)* and ketones *(9)* from the ylides *(1)* and *(8)* and the triphenylphosphite-ozone adduct *(2a)*.

R^1	R^2	*(7)* or *(9)*	Yield [%]
n-$C_{11}H_{23}$		12-Tetracosene	61
C_6H_6		Stilbene	89
p-CH_3O—C_6H_4		4,4'-Dimethoxystilbene	48
p-NO_2—C_6H_4		4,4'-Dinitrostilbene	72
$C_{19}H_{27}$ [a]		β-Carotene	75
CH_3—CO		1,2-Diacetylethylene	87
C_6H_5—CO		1,2-Dibenzoylethylene	62
CH_3O—CO		Dimethyl fumarate	83
C_6H_5	C_6H_5	Benzophenone	73
C_6H_5	CH_3	Acetophenone	77
C_6H_5CO	CH_3	Methyl phenyl diketone	81
C_6H_5CO	C_6H_5	Benzil	46

[a] R^1—CH_3 = axerophthene.

singlet oxygen ($^1O_2$)[5]. Decomposition of *(2a)* to triphenylphosphate *(3a)* and $^1O_2$ is shown by ^{31}P-NMR spectroscopy to proceed at a detectable rate only above −30 °C[1c], and that of the adduct *(2b)* of ozone and 4-ethyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane at 0 °C[1c] [^{31}P-NMR (toluene): *(2a)*: δ = +63.0; *(2b)*: +42.5; *(3a)*: +18.1; *(3b)*: +9.5; *(4)*: 24.1 ppm[6].

On combination of a salt-free solution of butylidenetriphenylphosphorane *(1)*, $R^1 = C_3H_7$, with *(2a)* or *(2b)* at −75 °C the ^{31}P-NMR spectrum recorded at that temperature contains no signal for *(2a)* or *(2b)*. Instead the signals of the phosphate *(3a)* or *(3b)* and of triphenylphosphane oxide *(4)* appear alongside those of a new compound containing pentavalent phosphorus at δ = +59.5 ppm[6] which we consider to be the initial cycloadduct formed in the Wittig reaction between *(1)* and *(5)* ($R^1 = C_3H_7$ in each case)[7] and to which we assign the structure of the oxaphosphetane *(6)*. In accord with this postulate a signal appears at the same position when *(1)*, $R^1 = C_3H_7$, is allowed to react with butyraldehyde *(5)*, $R^1 = C_3H_7$, at −75 °C. In both cases the intensity of the signal decreases as the temperature slowly rises until it has completely disappeared at 0 °C. The signal of *(4)* increases simultaneously.

General procedure:

A solution of *(2a)*[1a] in toluene or dichloromethane cooled to −70 to −80 °C is added dropwise to a stirred solution

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of the ylide *(1)* or *(8)* (preferably free from lithium) in toluene[8] (strongly basic ylides with R^1, R^2, R^3 = alkyl or aryl) or dichloromethane ("stable" ylides with R^1, R^2, or $R^3 = COR^4$), respectively, at the same temperature. The reaction mixture is then allowed to warm up to room temperature, any sodium halide that may have precipitated out is filtered off, and the solvent removed by distillation. Further workup depends on the properties of the olefins *(7)* or ketones *(9)*.

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CAS Registry numbers:
(1) ($R^1 = n\text{-}C_{11}H_{23}$), 54208-04-7; *(1)* ($R^1 = C_6H_5$), 16721-45-2; *(1)* ($R^1 = p\text{-}CH_3O\text{—}C_8H_4$), 21960-26-9; *(1)* ($R^1 = p\text{-}NO_2\text{—}C_6H_4$), 6933-17-1; *(1)* ($R^1 = C_{19}H_{27}$), 51283-60-4; *(1)* ($R^1 = CH_3\text{—}CO$), 1439-36-7; *(1)* $R^1 = C_6H_5\text{—}CO$), 859-65-4; *(1)* ($R^1 = CH_3O\text{—}CO$), 2605-67-6; *(2a)*, 29833-83-8; *(2b)*, 58594-17-5; *(3a)*, 115-86-6; *(3b)*, 1005-93-2; *(4)*, 13360-92-4; *(8)* ($R^1 = R^2 = C_6H_5$), 4214-38-4; *(8)* ($R^1 = C_6H_5$, $R^2 = CH_3$), 58594-19-7; *(8)* ($R^1 = C_6H_5CO$, $R^2 = CH_3$), 1450-07-3; *(8)* ($R^1 = C_6H_5CO$, $R^2 = C_6H_5$), 30416-76-3; 12-tetracosene, 58594-18-6; stilbene, 588-59-0; 4,4'-dimethoxystilbene, 4705-34-4; 4,4'-dinitrostilbene, 2501-02-2; β-carotene, 7235-40-7; 1,2-diacetylethylene, 4436-75-3; 1,2-dibenzoylethylene, 4070-75-1; dimethyl fumarate, 624-49-7; benzophenone, 119-61-9; acetophenone, 98-86-2; methyl phenyl diketone, 579-07-7; benzil, 134-81-6

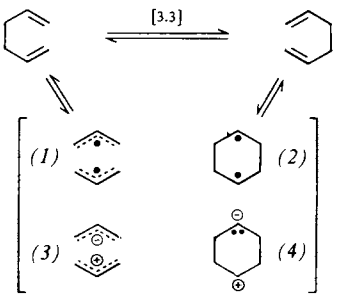
[1] a) *Q. E. Thompson*, J. Am. Chem. Soc. *83*, 845 (1961); b) *R. W. Murray* and *M. C. Kaplan*, *ibid. 91*, 5358 (1969); c) *M. E. Brennan*, Chem. Commun. *1970*, 956; d) *A. P. Schaap*, *A. L. Thayer*, *G. R. Faler*, *K. Goda*, and *T. Kimura*, J. Am. Chem. Soc. *96*, 4025 (1974).
[2] Cf. *H. J. Bestmann* and *H. Pfüller*, Angew. Chem. *84*, 528 (1972); Angew. Chem. Int. Ed. Engl. *11*, 508 (1972).
[3] *H. J. Bestmann* and *O. Kratzer*, Chem. Ber. *96*, 1899 (1963).
[4] Cf. *H. J. Bestmann* and *O. Kratzer*, Angew. Chem. *73*, 757 (1961); *H. J. Bestmann*, *O. Kratzer*, *R. Armsen*, and *E. Maekawa*, Justus Liebigs Ann. Chem. *1973*, 760.
[5] Compare the findings of *P. D. Bartlett* and *G. D. Mendenhall*, J. Am. Chem. Soc. *92*, 210 (1970); *A. P. Schaap* and *P. D. Bartlett*, *ibid. 92*, 6055 (1970), which appear to point in the same direction.
[6] 100-MHz PFT spectra, recorded between −90 and 0°C with triphenylphosphane oxide as internal standard and converted to 85% H_3PO_4 as external standard without correcting for the temperature dependence of the chemical shift (±0.3 ppm).
[7] *E. Vedejs* and *K. A. J. Snoble*, J. Am. Chem. Soc. *95*, 5778 (1973); *H. J. Bestmann* and *W. Downey*, unpublished; *W. Downey*, Diplomarbeit, Universität Erlangen-Nürnberg 1975; *M. Schlosser*, *A. Piskala*, *C. Tarchini*, and *H. B. Tuong*, Chimia *29*, 341 (1975).
[8] Preparation: *H. J. Bestmann*, Angew. Chem. *77*, 651 (1965); Angew. Chem. Int. Ed. Engl. *4*, 583 (1965); *H. J. Bestmann*, *W. Stransky*, and *O. Vostrowsky*, Chem. Ber., in press.

Cope Rearrangement with Dipolar Intermediates[**]

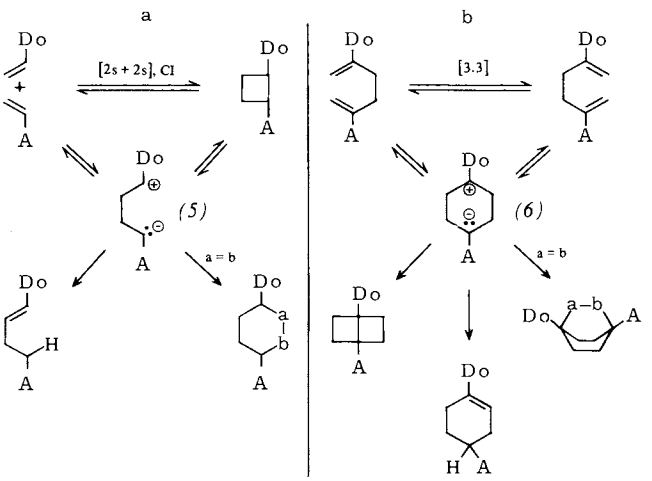
By *Rudolf Gompper* and *Wolf-Rüdiger Ulrich*[*]

The Cope rearrangement can be described either as a sigmatropic [3,3] rearrangement[1] or as a two-step process involving the intermediates *(1)*[2], *(2)*[3], *(3)*[4], or *(4)*.

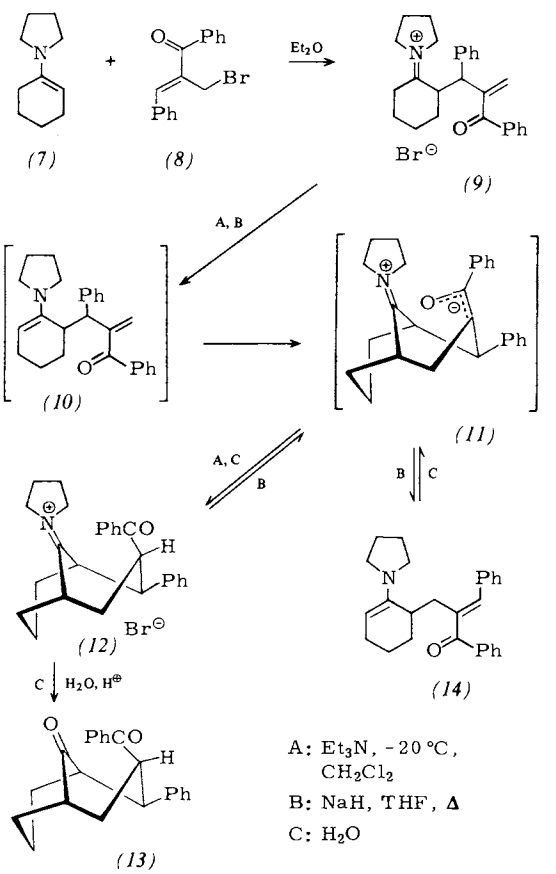
In connection with our studies on dipolar intermediates *(5)* in cycloadditions[5] we have attempted to stabilize intermediates of type *(4)* in Cope rearrangements by donor and acceptor groups and to detect them in the form of their derivatives *(6)* by means of typical reactions (Scheme 1b) such as are known for the (isolable) intermediates *(5)* in [2+2] cycloadditions (Scheme 1a). Polar Cope rearrangements according to Scheme 1b would provide a further entry to 1,4-dipoles and also document the significance of substituent



effects by the appearance of intermediates in symmetry-allowed pericyclic processes too. The α,α'-annelation of cyclic ketones[6] can be rationalized by the intermediacy of zwitterions of type *(6)*.



Scheme 1. Abbreviations: A = acceptor group; Do = donor group, CI = configurational interaction.



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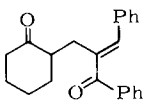
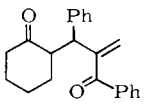
Reaction of *N*-(1-cyclohexenyl)pyrrolidine *(7)* with β-bromo-α-benzylidenepropiophenone *(8)* yields the salt *(9)* (m.p. 186—187 °C). Treatment of *(9)* with triethylamine (path A) provides an 80 % yield of the bicyclic immonium salt *(12)* (containing 1 mol of CH_2Cl_2: m.p. 237—239 °C), from which the ketone *(13)* (m.p. 104—105 °C) is obtained by acid hydrolysis.

Heating of the salts *(9)* and *(12)* with NaH in THF (path B) affords the enamino ketone *(14)* in both cases (yields *ca.* 80 and *ca.* 60 %, respectively). Treatment of *(14)* in THF with 70 % perchloric acid and subsequently with water produces the diketone *(15)* (b.p. 170 °C/10^{-3} torr).



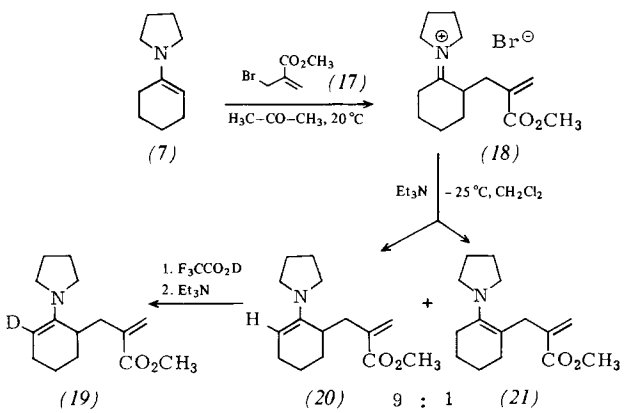
(15)



(16)

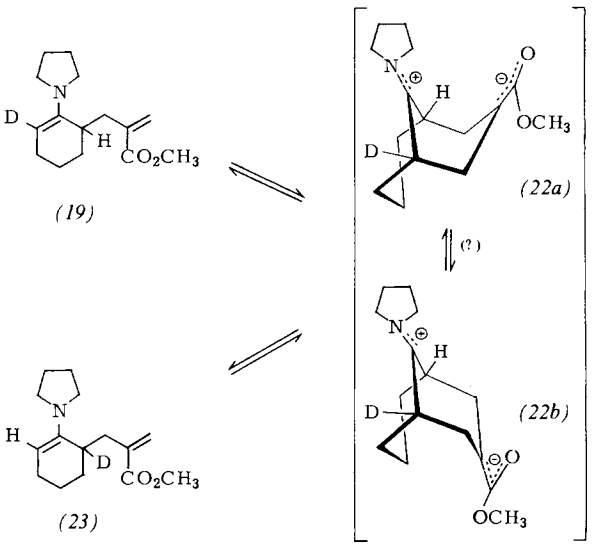
The isomeric diketone *(16)* (m.p. 120 °C) arises on acid hydrolysis of *(9)*.

Conversion of *(9)* into *(14)* by path B shows that the initially formed enamino ketone *(10)* has undergone a Cope rearrangement. The intermediacy of the zwitterion *(11)* in this rearrangement of *(10)* into *(14)* follows from formation of the bicyclic *(12)* from *(9) via* path A and of *(14)* from *(12) via* path B. This scheme of a two-step ("polar") Cope rearrangement is also compatible with the finding that the diketone *(13)* can be detected on treatment of *(14)* with water (path C).

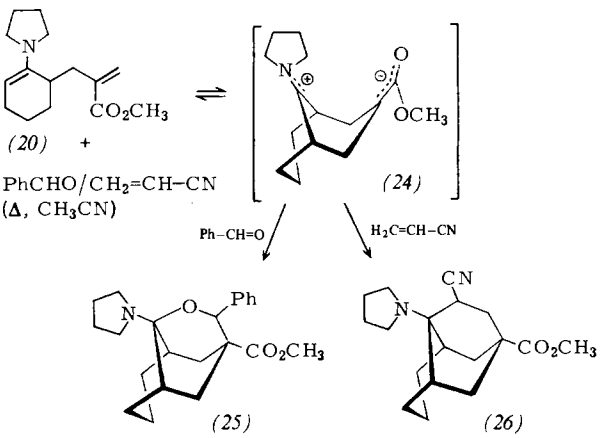


Since the enamino ketone *(10)* cannot be isolated we have attempted to synthesize similar polar Cope systems. The reaction of *(7)* with methyl bromomethacrylate *(17)* affords the salt *(18)* (m.p. 129—131 °C) in 75 % yield. On treatment of *(18)* with triethylamine a mixture of the enamines *(20)* and *(21)* is obtained in 80 % yield. Compound *(20)* can be purified by crystallization form *n*-pentane at −60 °C.

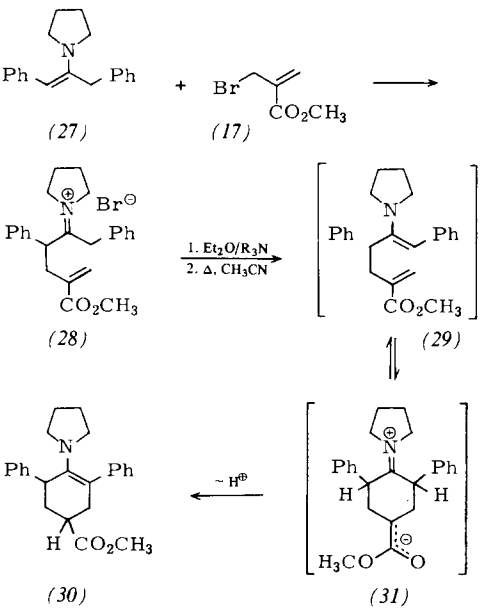
Deuteration of *(20)* is accomplished by treatment of its solution in dichloromethane at −20 °C (this temperature should not be exceeded throughout the entire operation) with an equimolar amount of deuteriotrifluoroacetic acid, addition of triethylamine after 30 min, removal of the solvent *in vacuo*, and dissolution of the residue in *n*-pentane. After filtration under N_2 the solvent is again removed *in vacuo*. The ^{1}H-NMR spectrum of the residue (in $[D]_8$-toluene) shows a drop in intensity of the triplet due to the ring vinyl proton at $\delta = 4.3$ ppm to 54 % relative to the signals of the other two vinylic protons at $\delta = 6.08$ and 5.3 ppm. On repetition of the procedure the intensity falls to 26 %, thus showing that *(19)* now predominates.



The Cope rearrangement can be detected in the 3 : 1 mixture of *(19)* and *(23)*. After 15 minutes' heating of a 1 % benzene solution the intensity of the triplet at $\delta = 4.3$ ppm has again risen to 45 %, and after four days' standing at room temperature to 55 %.



Proof of the dipolar intermediate *(22)* and the nondeuterated form *(24)* is obtained on heating of *(20)* with benzalde-



hyde and acrylonitrile. There result the cycloadducts *(25)* (yield 90%; m.p. 144—145°C) and *(26)* (yield 48%; m.p. 84—85°C).

A further possible reaction of intermediate *(6)* shown in Scheme 1 can be demonstrated by the action of tertiary amines in the immonium salt *(28)* obtained from *(17)* and *(27)* in ether at room temperature; yield 65%. Treatment of an ethereal solution of *(28)* with Hünig base (diisopropylethylamine) followed by decantation of the hydrobromide, evaporation of ether, and heating of the residue in acetonitrile permits isolation of the cyclic enamine *(30)* (yield 72%; m.p. 114—115°C), the species *(29)* and *(31)* presumably occurring as intermediates.

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CAS Registry numbers:
(7), 1125-99-1; *(8)*, 58703-26-7; *(9)*, 58703-27-8; *(10)*, 58703-28-9; *(12)*, 58703-29-0; *(13)*, 58703-30-3; *(14)*, 58703-31-4; *(15)*, 58703-32-5; *(16)*, 32528-28-2; *(17)*, 4224-69-5; *(18)*, 58703-33-6; *(19)*, 58703-34-7; *(20)*, 58703-35-8; *(21)*, 58703-36-9; *(23)*, 58703-37-0; *(25)*, 58703-38-1; *(26)*, 58703-39-2; *(27)*, 10321-68-3; *(28)*, 58703-40-5; *(30)*, 58703-41-6; deuteriotrifluoroacetic acid, 599-00-8; benzaldehyde, 100-52-7; acrylonitrile, 107-13-1

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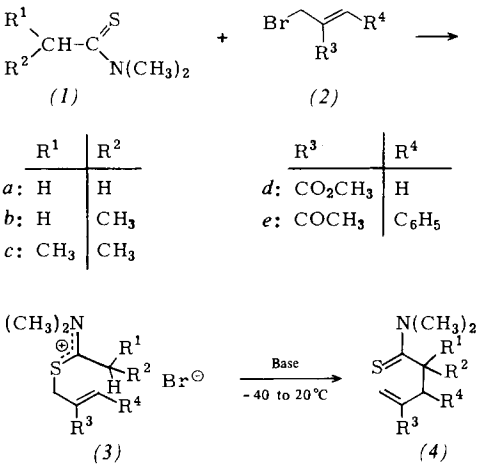
Hetero Cope Rearrangements with Dipolar Intermediates[**]

By *Rudolf Gompper* and *Wolf-Rüdiger Ulrich*[*]

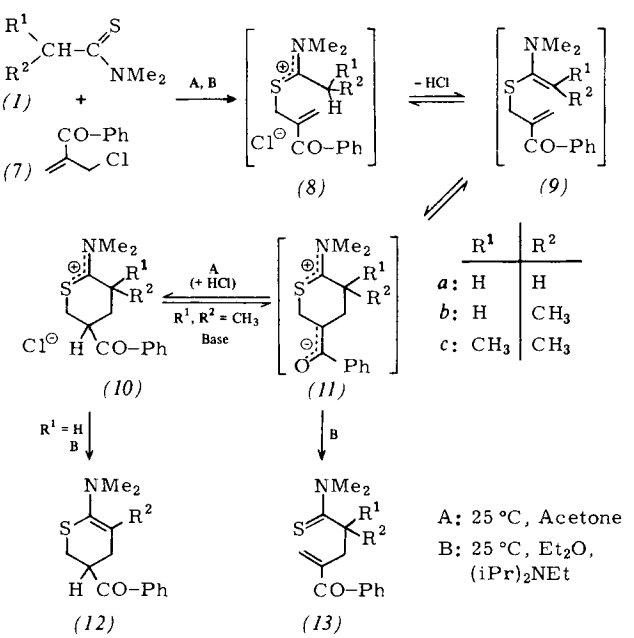
Cope rearrangements of 1,5-hexadienes bearing a donor group in position 2 and an acceptor group in position 5 are much faster than the rearrangements of compounds with "neutral" groups in these positions, and 1,4-dipolar intermediates can be detected[1]. The rate of hetero Cope rearrangements is also enhanced by the presence of donor-acceptor groups (cf. ref. [2]): The thioamides *(1)* and the allyl bromides *(2)* afford (ether, reflux) the salts *(3)* in excellent yields [*(3ad)*: m.p. 98—100°C; *(3bd)*: m.p. 113—114°C; *(3cd)*: m.p. 93—94°C; *(3ae)*: m.p. 103—105°C (dec.); *(3be)*: m.p. 126—127°C]. Treatment of solutions of *(3)* in acetonitrile (−40°C) or their suspensions in ether (20°C) with diisopropylethylamine (NaH in THF can also be used) furnishes the thioamides *(4)* in 60—80% yield [*(4ad)*: m.p. 18—20°C; *(4bd)*: b.p. 94—95°C/0.5 torr; *(4cd)*: b.p. 75°C/0.5 torr; *(4ae)*: m.p. 77—79°C; *(4be)*: m.p. 126—127°C].



	R^1	R^2
a:	H	H
b:	H	CH_3
c:	CH_3	CH_3

	R^3	R^4
d:	CO_2CH_3	H
e:	$COCH_3$	C_6H_5

Proof of the intermediacy of dipolar species in these thia Cope rearrangements has been obtained in the reactions of *(1)* with α-chloromethylacrylophenone *(7)*: reaction at room temperature in acetone (path A) gives the cyclic salts *(10)* [*(10a)*: yield 50%; m.p. 150—152°C; *(10b)*: yield 65%; m.p. 96—98°C; *(10c)*: yield 60%; m.p. 175—176°C]. Under otherwise identical conditions in the presence of diisopropylethylamine (path B) one obtains the thioamides *(13)* [*(13a)*: yield 40% based on *(7)*; b.p. 150°C/10^{-3} torr; *(13b)*: yield 60%; b.p. 150°C/10^{-3} torr; *(13c)*: yield 70%].



	R^1	R^2
a:	H	H
b:	H	CH_3
c:	CH_3	CH_3

These results can be interpreted by assuming *(1)* and *(7)* to initially form the quaternary salts *(8)* which are transformed by deprotonation into the thia Cope systems (ketene *S,N*-acetals) *(9)*. "Cope cyclization" of *(9)* affords the 1,4-dipoles *(11)*, which in the absence of a strong base are trapped by the hydrogen chloride present in the reaction mixture to form *(10)*. Protonation of *(11)* fails to occur in the presence of diisopropylethylamine; instead the ring is opened to give *(13)*.

This scheme is compatible with the finding that the action of bases (*e.g.* diisopropylethylamine) on *(11c)* also leads to *(13)*. Thus it is established that the 1,4-dipoles *(11)* occur as intermediates in the thia Cope rearrangement of *(9)* to *(13)*.

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It is remarkable that the deprotonation of *(10)* can also follow a different route. Treatment of the solutions of *(10a)* and *(10b)* in ether with diisopropylethylamine gives good yields of the cyclic ketene *S,N*-acetals *(12)* [*(12a)*: b.p. 150°C/10^{-3} torr; *(12b)*: b.p. 125°C/10^{-3} torr].

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CAS Registry numbers:
(1a), 631-67-4; *(1b)*, 5309-94-4; *(1c)*, 52912-63-7; *(2d)*, 4224-69-5; *(2e)*, 58702-91-3; *(3ad)*, 58702-92-4; *(3bd)*, 58702-93-5; *(3cd)*, 58702-94-6; *(3ae)*, 58702-95-7; *(3be)*, 58702-96-8; *(4ad)*, 58702-97-9; *(4bd)*, 58702-98-0; *(4cd)*, 58702-99-1; *(4ae)*, 58703-00-7; *(4be)*, 58703-01-8; *(7)*, 58703-02-9; *(10a)*, 58703-03-0; *(10b)*, 58703-04-1; *(10c)*, 58703-05-2; *(12a)*, 58703-06-3; *(12b)*, 58703-07-4; *(13a)*, 58703-08-5; *(13b)*, 58703-09-6; *(13c)*, 58703-10-9

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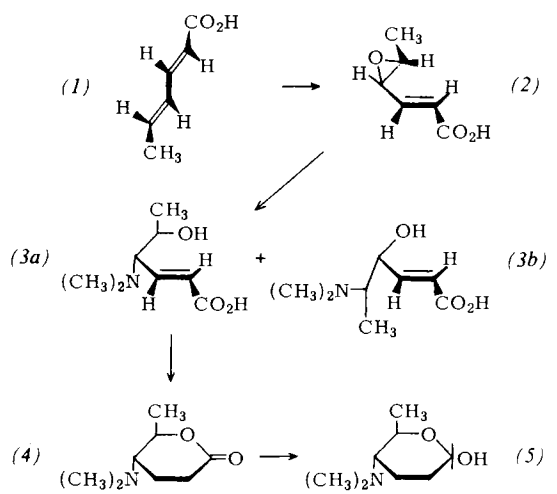
Synthesis of D-Forosamine, the 4-Dimethylamino Sugar from Spiramycin[1][**]

By *Ingolf Dyong, Rainer Knollmann*, and *Norbert Jersch*[*]

Little is known about the biological function of the often rather unusual sugars present in antibiotics[2]; a prerequisite for model studies is to be seen in the availability of productive syntheses.

Forosamine, the 4-dimethylamino-2,3,4,6-tetradeoxy-D-*erythro*-hexose *(5)* which occurs alongside mycarose and mycaminose in spiramycin, a therapeutically employed macrolide antibiotic complex from *Streptomyces ambofaciens*[3], is accessible only with great difficulty *via* two earlier syntheses each involving thirteen steps in yields of 0.1[4] and 1%[5], respectively.

We have found an alternative synthetic pathway of general significance for the preparation of neutral and basic polydeoxyhexoses[6] which provides a ready entry to *(5)*.



Epoxidation of sorbic acid *(1)* with 40% peracetic acid affords the enantiomeric *trans*-4,5-epoxy-*threo*-2-hexenoic acids (yield 76%) of which the D-isomer *(2)* crystallizes from ether (yield 90%) with D-(+)-phenylethylamine. Compound *(2)* [m.p. 82—84°C, $[\alpha]_D^{22} = +7.6°$ ($c = 1.0$, $CHCl_3$), yield 98%], liberated on treatment of the ammonium salt with dilute acid, reacts with 40% aqueous dimethylamine at room temperature to give a 4:1 mixture of 4-dimethylamino-5-hydroxy-D-*erythro*-2-hexenoic acid *(3a)* and 5-dimethylamino-4-hydroxy-L-*erythro*-2-hexenoic acid *(3b)* (yield 87%), from which the 4-dimethylamino lactone *(4)* [$[\alpha]_D^{25} = +116.2°$ ($c = 1.2$, benzene), yield 61%] can be isolated with acetone/benzene/dioxane (1:1:1) after catalytic hydrogenation and lactonization with acetic anhydride. Reduction of *(4)* with diisobutylaluminum hydride in tetrahydrofuran at −30°C furnishes forosamine *(5)*, obtained as a syrup from acetone. It rapidly crystallizes [m.p. 58—60°C, $[\alpha]_D^{25} = +86.1°$ ($c = 0.9$, methanol), yield 70%[7]].

Apart from M^+ (14%), a key fragment in the mass spectrum of *(5)* is the K_1 ion $[(CH_3)_2N{-}CH{=}CH{-}CH_3]^+$ (14%).—The yield of *(5)* from *(1)* is 25%, considering only the D-isomer *(2)*.

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CAS Registry numbers:
(1), 110-44-1; *rac.-(2)*, 58692-58-3; *(2)*, phenylethylamine salt, 58717-78-5; *(2)*, 58717-79-6; *(3a)*, 58692-59-4; *(3b)*, 58692-60-7; *(4)*, 22882-12-8; *(5)*, 18423-27-3; peracetic acid, 79-21-0; D-(+)-phenylethylamine, 3886-69-9

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[6] *I. Dyong* and *N. Jersch*, Chem. Ber. *109*, 896 (1976).
[7] *(5)* from spiramycin: m.p. 60°C, $[\alpha]_D^{23} = +83.9°$ ($c = 1$, methanol) (*R. Paul* and *S. Tchelitcheff*, Bull. Soc. Chim. Fr. *1957*, 734). Ref. [5]: m.p. 58—60°C, $[\alpha]_D^{25} = +90.0 \pm 1°$ ($c = 1$, methanol); the NMR data given in ref. [5] agree with those of our synthetic *(5)*.

Stereospecific Synthesis of β-Bromoamines by Ionic Addition of Diethyl Dibromophosphoramidate to a Double Bond[**]

By *Andrzej Zwierzak* and *Krystyna Osowska*[*]

While free-radical addition of various *N,N*-dihaloamides to double bonds has been extensively studied over the past decade[1], the available information about ionic reactions of such systems with unsaturated compounds remains scarce and inadequate[2].

In the course of our studies on the possible application of diethyl dibromophosphoramidate *(1)* for regiospecific functionalization of a double bond[3] we have found that this reagent readily adds to unsaturated hydrocarbons such as styrene or cyclohexene. When the reaction is carried out in carbon tetrachloride at −20°C in the presence of stoichiometric amounts of trifluoroborane-ether it affords *N*-bromo-*N*-(β-bromoalkyl)phosphoramidates which can be readily reduced

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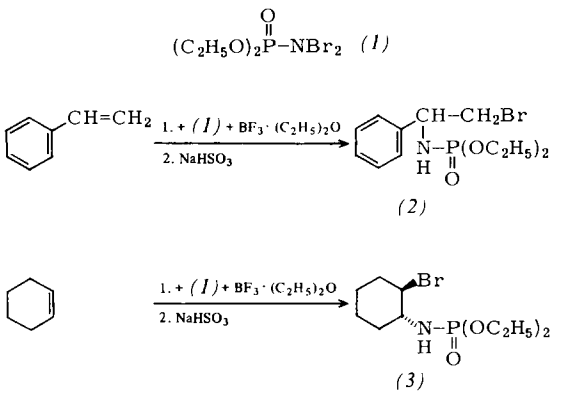
[+] Author to whom correspondence should be addressed.

[**] *N,N*-Dihalophosphoramides, Part 11.—Part 10: *A. Koziara* and *A. Zwierzak*, Tetrahedron, in press.

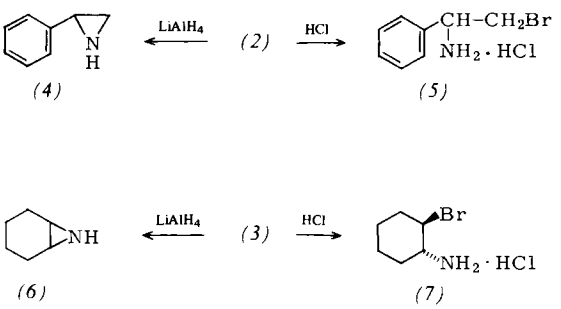


with 20% aqueous sodium hydrogen sulphite to the *N*-(β-bromoalkyl)phosphoramidates *(2)* and *(3)*.

Compound *(2)* [92% yield, m.p. 90—91 °C (*n*-hexane)], which evidently was formed by ionic, Markovnikov addition, was found to be uncontaminated by other regioisomers[4]. The structure of *(3)* [m.p. 79—81 °C (*n*-hexane)] was deduced from its IR and ^{1}H-NMR spectra and also the spectra of its degradation product *(7)*. From the spectra of *(7)* it would appear that both ring substituents are located in *trans*-diequatorial positions. The observed stereospecificity of the addition is fully consistent with the ionic course predicted for this reaction.

Both adducts *(2)* and *(3)* can be readily transformed into the corresponding aziridines *(4)* and *(6)*[5] in 79 and 72% yield respectively[6] by the action of lithium aluminum hydride in ether.

(2) and *(3)* are easily converted into the corresponding β-bromoamines *(5)* and *(7)* by the action of gaseous hydrogen chloride in THF at room temperature (24 h, yields 95 and 90%, respectively).



The reaction sequence: olefin → *(1)*-adduct → β-bromoamine hydrochloride, which can be realized in excellent overall yield, offers an attractive approach to functionalization of a double bond on account of its simplicity, mild reaction conditions, lack of side-products, and predictable regio- and stereospecificity.

Procedure:

Trifluoroborane-ether (7.1 g, 0.05 mol) was added dropwise with stirring to a solution of *(1)*[3a] (15.5 g, 0.05 mol) in CCl_4 (100 ml) at −20 °C. The olefin (0.05—0.06 mol) was then added and the mixture heated slowly to 20 °C. 30 ml of a 20% aqueous solution of $NaHSO_3$ was added dropwise at this temperature and the organic layer separated, washed with water (2 × 50 ml), dried and evaporated *in vacuo* to give crude adduct *(2)* or *(3)* as a hard, crystalline mass. For the degradation a solution of *(2)* or *(3)* (0.03 mol) in THF (25 ml) was saturated with gaseous HCl and set aside at room temperature for 24 h. The crystals of *(5)* or *(7)* were then filtered off, washed with ether, and recrystallized from ethanol/ether (2:1).

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(1), 32755-13-8; *(2)*, 58692-61-8; *(3)*, 58692-62-9; *(4)*, 1499-00-9; *(5)*, 58692-63-0; *(6)*, 286-18-0; *(7)*, 58692-64-1; styrene, 100-42-5; cyclohexene 110-83-8

[1] *R. S. Neale*, Synthesis *1971*, 1; and references cited therein.
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Correlation between the β-Effect of Methyl Groups on $\delta(^{13}C)$ and the C_α—C_β π-Bond Order[**][1]

By *Ludger Ernst*[*]

A knowledge of the influence of substituents on chemical shifts is often the most important prerequisite for an unambiguous interpretation of ^{13}C-NMR spectra. We report here on the β-effect of methyl groups on $\delta(^{13}C)$, *i.e.* on the change, $\Delta\delta_\beta$, of the shift of C_β in going from *(1)* to *(2)*.

(1) $H-C_\alpha=C_\beta \longrightarrow CH_3-C_\alpha=C_\beta$ *(2)*

In an investigation of the ^{13}C spectra of the isomeric monomethylcoumarins[2] we suggested for the first time, that a relationship existed between $\Delta\delta_\beta$ and the bond order P_π between the $2p_z$ orbitals of atoms C_α and C_β, which we had calculated by the INDO-MO method[3] (cf. Table 1, cases 10, 11, 16, 21). In the meantime we have been able to substantiate the correlation between $\Delta\delta_\beta$ and P_π. Regression analysis of the data in Table 1 affords the relationship

$$\Delta\delta_\beta\ [\text{ppm}] = 12.6 - 18.6\,P_\pi \qquad \text{(a)}$$

(correlation coefficient −0.985, rms deviation 0.68 ppm). Since introduction of a methyl group has only a slight influence on the bond orders, it is irrelevant whether equation (a) is derived from the bond orders of *(1)* or from those of *(2)*[4].

Qualitatively, equation (a) implies that a high C_α—C_β π-bond order results in a large shielding β-effect of the methyl group (cf. propene/ethylene) and that low bond orders cause large deshielding β-effects, whereas only small β-(=*ortho*-) effects occur in the case of intermediate π-bond orders (cf. toluene/benzene).

In terms of the Karplus-Pople theory of ^{13}C shifts[5], whose very approximate nature ought to be borne in mind, the observed relation could be interpreted in such a way that

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of the applicable parameters (ΔE, $\langle r^{-3}\rangle_{2p}$, $\sum_B Q_{AB}$) mainly the latter is affected by the replacement of H by methyl. This parameter is a summation of bond order terms, in which the change of P_π (C_α—C_β) should play the principal role in going from *(1)* to *(2)*. In order to arrive at an equation of type (a), the change of P_π must, moreover, be proportional to the magnitude of P_π in *(1)*. For the time being we wish to emphasize the empirical nature of the relationship.

Table 1. Comparison of experimental and calculated [Eq. (a)] β-effects [ppm] of methyl groups on $\delta(^{13}C)$.

Case [a]	P_π	$\Delta\delta_\beta$(exp.) [b]	$\Delta\delta_\beta$(calc.)	Deviation
1	0.145	9.6	9.86	−0.26
2	0.174	9.7	9.33	0.37
3	0.194	8.7	8.95	−0.25
4	0.496	3.1	3.35	−0.25
5	0.501	4.04	3.26	0.78
6	0.530	2.3	2.71	−0.41
7	0.538	1.54	2.57	−1.03
8	0.642	0.50	0.64	−0.14
9	0.642	0.62	0.64	−0.02
10	0.653	1.18	0.43	0.75
11	0.653	0.96	0.43	0.53
12	0.664	0.77	0.23	0.54
13	0.664	0.36	0.23	0.13
14	0.664	−0.43	0.23	−0.66
15	0.667	0.64	0.17	0.47
16	0.668	0.15	0.14	0.01
17	0.671	0.34	0.09	0.25
18	0.671	−0.75	0.09	−0.84
19	0.671	−0.85	0.09	−0.94
20	0.679	−0.53	−0.06	−0.47
21	0.683	−0.20	−0.12	−0.08
22	0.701	0.70	−0.47	1.17
23	0.701	−0.50	−0.47	−0.03
24	0.782	−1.0	−1.97	0.97
25	0.784	−1.92	−2.00	0.08
26	0.784	−1.86	−2.00	0.14
27	0.806	−1.6	−2.41	0.81
28	0.850	−4.03	−3.22	−0.81
29	0.947	−3.6	−5.03	1.43
30	0.947	−5.2	−5.04	−0.16
31	0.947	−5.7	−5.04	−0.66
32	1.000	−7.4	−6.02	−1.38

[a] The Case Numbers refer to the following methyl compounds; the C-atom in the β-position to the methyl groups is given in brackets. 1: methylcyclopropane (C-2); 2: propane (C-1); 3: 3-methylcyclopropene (C-1); 4: 2-methylanthracene (C-3); 5: *N*-methylpyrrole (C-2); 6: 2-methylnaphthalene (C-3); 7: 3-methylpyrrole (C-4); 8: 4-methylpyridinium ion (C-3); 9: 3-methylpyridinium ion (C-4); 10: 7-methylcoumarin (C-6); 11: 6-methylcoumarin (C-7); 12: 4-methylpyridine (C-3); 13: 3-methylpyridine (C-4); 14: 3-methylpyrazole (C-4); 15: toluene (C-2); 16: 7-methylcoumarin (C-8); 17: 3-methylpyridine (C-2); 18: 2-methylpyridine (C-3); 19: 4-methylpyrimidine (C-5); 20: 2-methylpyrazine (C-3); 21: 6-methylcoumarin (C-5); 22: 2-methylpyridinium ion (C-3); 23: 3-methylpyridinium ion (C-2); 24: 2-methylnaphthalene (C-1); 25: 2-methylpyrrole (C-3); 26: 3-methylpyrrole (C-2); 27: 2-methylanthracene (C-1); 28: 2-methylfuran (C-3); 29: crotonaldehyde (C-2); 30: crotonic acid (C-2); 31: methacrylic acid (C-3); 32: propene (C-1).
[b] Own measurements are given to two decimal places; the other values are from Ref. [6].

The usefulness of equation (a) for signal assignments is obvious. The relationship is certainly most useful for the interpretation of the ^{13}C spectra of molecules with bonds of widely differing double-bond character, *e.g.* of polycyclic or heterocyclic aromatics, even if quantitative predictions cannot be expected (see Table 1). Recently, the difficulty of assigning the signals of C-2 and C-5 in the spectrum of 3-methylfuran was reported[7]. Depending on how these signals are assigned, a β-effect of the methyl group on δ_2 with a value of +0.1 or of −3.2 ppm would result. For an unequivocal decision, rather involved double-resonance experiments had to be carried out. Equation (a) would have predicted −3.21 ppm for $\Delta\delta_2(P_\pi^{2,3}$ in furan: 0.85) and would thus have easily distinguished between the two possibilities.

When interfering steric effects are present, *e.g.* in *ortho*-substituted methyl aromatics, equation (a) is no longer a good approximation; the discrepancies which then occur demand further investigation.

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(1), 594-11-6; *(2)*, 74-98-6; *(3)*, 18631-90-8; *(4)*, 613-12-7; *(5)*, 96-54-8; *(6)*, 91-57-6; *(7)*, 616-43-3; *(8)*, 16950-21-3; *(9)*, 17203-41-7; *(10)*, 2445-83-2; *(11)*, 92-48-8; *(12)*, 108-89-4; *(13)*, 108-99-6; *(14)*, 1453-58-3; *(15)*, 108-88-3; *(18)*, 109-06-8; *(19)*, 3438-46-8; *(20)*, 109-08-0; *(22)*, 16969-46-4; *(25)*, 636-41-9; *(28)*, 534-22-5; *(29)*, 4170-30-3; *(30)*, 3724-65-0; *(31)*, 79-41-4; *(32)*, 115-07-1

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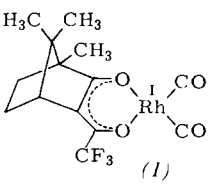
Separation of Deuteriated Ethylenes $C_2H_{4-n}D_n$ by Complexation Chromatography on a Rhodium(I) Complex[**]

By *Volker Schurig*[*]

Separations of deuteriated or ^{11}C and ^3H doubly-labeled alkenes have been carried out gas chromatographically on $AgNO_3$/ethylene glycol[1]. However, despite extreme conditions (75 m-long packed columns, recycling[1]) the separation of isotopes differing by only one mass unit was only partly successful. Moreover, $AgNO_3$ phases prove to have only a limited lifetime.

We have observed a considerably greater secondary isotope effect for $[D_4]/[D_0]$-ethylenes on the highly alkene-selective rhodium(I) β-diketonate phases previously described by us, *e.g.* dicarbonylrhodium(I) 3-trifluoroacetylcamphorate *(1)*[2]



(1)

in squalane, than on silver(I)[3]; their quantitative separation is already possible with a 2 m-long packed column. In contrast to $AgNO_3$, *(1)* is also suitable for the coating of high-resolution capillary columns having high separation efficiency and stability[4].

We have now been able to separate all deuteriated ethylenes $C_2H_{4-n}D_n$ under simple experimental conditions by complexation chromatography on rhodium(I) in 75 min at 22 °C (Fig. 1). The logarithmically additive separation factors $\alpha = t_D/t_H$

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measured at several temperatures [α (22 °C) = (1.055)^n, α (42 °C) = (1.050)^n, and α (63 °C) = (1.042)^n, n = number of deuterium atoms] and the thermodynamic parameters of the π-complexing of [D_4]-/[D_0]-ethylene with *(1)* [$K_D/K_H = 1.28$ (22 °C), 1.24 (42 °C) and 1.21_5 (63 °C), $(\Delta H_D - \Delta H_H) = -0.24 \pm 0.01$ kcal/mol and $(\Delta S_D - \Delta S_H) = -0.34 \pm 0.04$ cal K^{-1} mol^{-1}] are the highest values observed so far for "inverse" ($K_D > K_H$) secondary isotope effects.

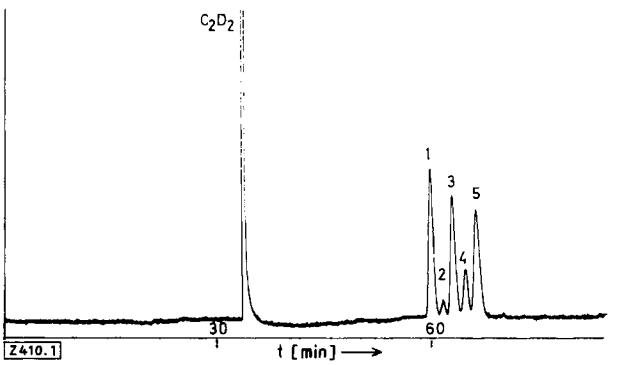

Fig. 1. Complexation chromatogram of the deuteriated ethylenes $C_2H_{4-n}D_n$ on *(1)* at 22 °C. 1: C_2H_4, 2: C_2H_3D, 3: $C_2H_2D_2$ (all isomers), 4: C_2HD_3, 5: C_2D_4.

Similarly selective separations are to be expected for deuteriated propenes or isomeric butenes. A doubling of the separation factors can be anticipated in the case of tritiated alkenes.

Procedure:

A 200 m × 0.5 mm steel capillary column (previously cleaned with HNO_3) is coated with a solution of *(1)*[2] (4 mg) in squalane (250 mg) diluted with CH_2Cl_2 (5 ml) at 1.75 atm N_2 (pure) and then conditioned for 150 h at 3 atm N_2 (n = 160000, isooctane) in the gas chromatograph (Carlo-Erba, Fractovap 2101). To avoid peak-tailing the separation is carried out at the highest sensitivity (output × 2), 1 µl gas mixture, split 1:100, column throughput 1.2 ml N_2/min, FID (100 °C, externally heated). The phase remains active over a period of months in absence of oxygen.

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CAS Registry numbers:
(1), 36654-16-7

[1] *J. G. Atkinson, A. A. Russell,* and *R. S. Stuart,* Can. J. Chem. *45*, 1963 (1967); and literature cited therein.
[2] *V. Schurig,* Inorg. Chem. *11*, 736 (1972).
[3] *V. Schurig* and *E. Gil-Av,* Chem. Commun. *1971*, 650; *E. Gil-Av* and *V. Schurig,* Anal. Chem. *43*, 2030 (1971).
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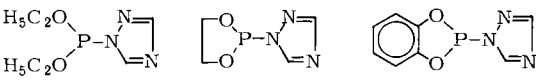
Synthesis of (Poly-)Peptides with Phosphorous Diester Triazolides[**]

By *Hans R. Kricheldorf, Martin Fehrle,* and *Jürgen Kaschig*[*]

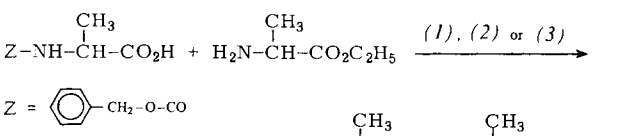
Reaction of 1-(trimethylsilyl)-1,2,4-triazole[1] with the phosphorous chlorides diethyl phosphorochloridite, 2-chloro-1,3,2-dioxaphospholane, and 2-chloro-1,3,2-benzodioxaphosphole leads to the phosphorous diester triazolides *(1)*, *(2)*, and *(3)*, respectively. They react readily with water, alcohols, carboxylic acids, and amines, are easy to isolate, and can be stored in a dry place.

N-Protected amino acids and amino acid alkyl esters can be condensed with *(1)*, *(2)*, or *(3)* to give peptides, *e.g.* *(4)*, in 70—80% yields. No crystalline products could be

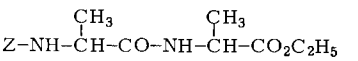


(1) *(2)* *(3)*

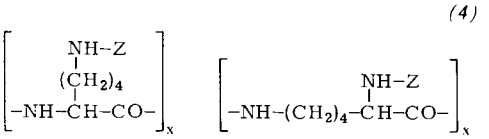
obtained in experiments on the esterification of Z-alanine with 4-nitrobenzyl alcohol or of Z-β-alanine with *tert*-butyl glycolate. Unlike many other condensation reagents, the triazolides *(1)*—*(3)* also react smoothly in polar solvents with free amino acids or oligopeptides to yield polypeptides and polyamides. Thus N^{ε}-Z-lysine affords the polypeptide *(5)*, which, like the polymers mentioned here, was characterized by elemental analysis, IR spectroscopy, and NMR spectroscopy (220 MHz in CF_3CO_2H). In addition, *(5)* was compared with a polymer which had been obtained by amine-catalyzed polymerization of N^{ε}-Z-lysine-N^{α}-carboxylic acid anhydride. Both polymers exhibited comparable rotations, thus indicating that no appreciable racemization takes place in the polycondensation with *(1)*—*(3)* below 80 °C.



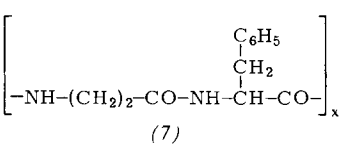
Z = Z-O-CO



(4)



(5) *(6)*



(7)

$[-NH-A-CO-NH-CH_2-CO-NH-CH_2-CO-]_x$

(8), A = $-CH(CH_2C_6H_5)-$; *(9)*, A = $-CH_2-CH_2-$;
(10), A = $-CH(CH_3)-$

N^{α}-Z-isopolylysine *(6)* and poly[β-Ala-Phe] *(7)* prepared with *(1)* were likewise identified by comparison with polypeptides which had been obtained by polycondensation of N^{α}-Z-lysine- and β-Ala-Phe-pentachlorophenyl ester trifluoroacetates, respectively. The sequence polypeptides *(8)*, *(9)*, and *(10)* could also be prepared from Phe-Gly-Gly, β-Ala-Gly-Gly and Gly-Gly-D,L-Ala, respectively, with *(1)*.

The crude products of the polycondensation with *(1)*—*(3)* had to be freed from attendant phosphorous acid derivatives. In the case of water-insoluble polymers [*(5)*—*(9)*] this was accomplished by boiling with 5% ammonia solution and methanol, and in the case of the water-soluble polypeptide

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(10) by boiling with ammonia followed by dialysis. Compound *(3)*, which proved to be especially reactive in polycondensations, gave rise to most contaminants; consequently, *(1)* and *(2)* are to be preferred. As comparative experiments for the synthesis of *(6)* have shown, the same problem of purification occurs in the case of the less reactive condensation agents such as triphenyl phosphite or diphenyl phosphite.

Phosphorous diester triazolides (1)—(3)

1-(Trimethylsilyl-1,2,4-triazole (1.0 mol) and the corresponding phosphorous diester chloride of *(1)—(3)* (1.0 mol) are mixed in dry benzene (100 ml) and heated to boiling for 10 min. The major portion (*ca.* 60 %) of trimethylchlorosilane and benzene is then slowly distilled off *via* a Claisen head filled with glass wool, and any residual volatile products removed in a vacuum. *(1)* and *(2)* are isolated by distillation; the oily crude *(3)* is washed with a fivefold amount of warm petroleum ether and then cooled to 0 °C, whereupon it crystallizes almost completely.—1-(Diethoxyphosphino)-1,2,4-triazole *(1)*, yield 91 %, b.p. 75—77 °C/0.01 torr, $n_D^{20} = 1.4710$; 1-(1,3,2-dioxaphospholan-2-yl)-1,2,4-triazole *(2)*, yield 81 %, b.p. 74—76 °C/0.01 torr, $n_D^{20} = 1.5263$; 1-(1,3,2-benzodioxaphosphol-2-yl)-1,2,4-triazole *(3)*, yield 91 %, m.p. 55—57 °C.—*(3)* could not be subjected to elemental analysis because of its sensitivity to hydrolysis. In the case of *(2)* spontaneous ignition of the residue occurred within a few minutes of opening the warm distillation apparatus.

N-Benzyloxycarbonylalanylalanine ethyl ester (4)

A mixture of Z-L-Ala (0.1 mol) and *(1)* (0.1 mol) in dry dimethylformamide (50 ml) is stirred for 30 min. Addition of 0.1 mol L-alanine ethyl ester hydrochloride is followed by dropwise addition of 0.1 mol *N*-methylmorpholine. After about 12 h the reaction mixture is stirred together with a mixture of 250 ml water, a few drops of hydrochloric acid, and 300 ml ethyl acetate; the organic phase is separated off, dried, and evaporated to dryness. The product *(4)* crystallizes out on treatment with carbon tetrachloride and petroleum ether under cooling; yield 76 % [with *(2)*: yield 79 %; with *(3)*: yield 73 %], m.p. 113—115 °C (ref. [2]: 116 °C).

Poly β-Ala-L-Phe (7)

A mixture of finely powdered β-Ala-L-Phe (0.05 mol) in dry dimethylformamide (50 ml) is warmed with stirring to 80 °C, whereupon a part of the dipeptide goes into solution; after 30 min the polymer *(7)* begins to precipitate out. After four days at 80 °C the reaction mixture is stirred with 300 ml 1 N HCl; the precipitated polypeptide *(7)* is boiled for 4 h with a 5 % ammonia solution and 1 h with methanol; yield 50 %. ^{1}H-NMR (CF_3COOH): δ = 2.64, 3.11, 3.53, 4.82, 7.18, 7.30, 7.77, 8.00 ppm (2:2:2:1:2:3:1:1).

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CAS Registry numbers:
(1), 58673-12-4; *(2)*, 58673-13-5; *(3)*, 58673-14-6; *(4)*, 5673-69-8; *(7)* (repeating unit), 32146-14-8; *(7)* (polymer), 31986-99-9; 1-(trimethylsilyl)-1,2,4-triazole, 18293-54-4; diethyl phosphorochloridite, 589-57-1; 2-chloro-1,3,2-dioxaphospholane, 822-39-9; 2-chloro-1,3,2-benzodioxaphosphole, 1641-40-3; Z-L-Ala, 1142-20-7; β-Ala-L-Phe, 17136-28-6

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Regioselective Chlorination of Centered Methylene Groups in Dicarboxylic Acids[**]

By *Friedhelm Kämper, Hans J. Schäfer*, and *Heinrich Luftmann*[*]

We are presently studying the feasibility of regioselectively functionalizing unactivated C—H bonds remote from functional groups by electrostatic orientation of the reagent.

According to *Deno*[1] 1-hexanol, hexyl methyl ether, and hexanoic acid are chlorinated up to more than 90 % in the (ω − 1) position when treated with *N*-chlorodiisopropylamine in sulfuric acid (concentration: 72 %, 84 %, and 84 %, respectively). We have found that the C_6- to C_{12}-diacids are photochlorinated regioselectively at methylene groups situated in the middle of the chain with this reagent in sulfuric acid (Table 1).

In this radical chain substitution[3] the protonated CO_2H groups[4] could conceivably direct the H-withdrawing diisopropylamine radical cation electrostatically into the middle of the dicarboxylic acid.

Table 1. Chlorination of dicarboxylic acids with *N*-chlorodiisopropylamine in sulfuric acid.

	H_2SO_4 conc. [wt. %]	Distribution of isomers of the monochlorinated dicarboxylic acids [%] [a] α	β	γ	δ	ε	Conversion [%] [b]	Polychlorinated dicarboxylic acids [%] [a]
Hexanedioic acid	85	4	96				2	0
Heptanedioic acid	85	0	3	97			11	0
Octanedioic acid	73	0	21	79				
Octanedioic acid	85	0	4	96			45	1
Nonanedioic acid	85	0	2	40	58		72	3
Decanedioic acid	73	0	3	20	77			
Decanedioic acid	85	0	1	14	85		96	4
Decanedioic acid	95	0	< 0.5	11.5	88			
Dodecanedioic acid	85	0	< 0.5	2	32	66	96	5
Dodecanedioic acid	95	0	0	0.5	27	72		

[a] Determined gas chromatographically (4 % ethylene succinate on Chromosorb W) *via* the dimethyl ester [2].
[b] Determined gas chromatographically.

The structure of the isomers was assigned mass spectrometrically and NMR spectroscopically using the shift reagent $Eu(fod)_3$. For the mass spectroscopic characterization the iso-

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meric chlorodicarboxylic acids were converted into the dimethylamino derivatives in order to obtain a specific fragmentation. For example, the methyl esters of the isomeric dimethylaminodecanedioic acids cleave into the characteristic fragments: *m/e* 158, 172 (δ), 186, 144 (γ), 200, 130 (β). The CHCl proton of the dimethyl ester of the predominantly occurring chlorodecanedioic acid shows the same shift as the δ-CH_2 proton of unsubstituted dimethyl decanoate at various $Eu(fod)_3$ concentrations.

Experimental:

A solution of *N*-chlorodiisopropylamine (50 mmol) and decanedioic acid (50 mmol) in 85 % sulfuric acid (80 ml) under nitrogen is irradiated (Hg high-pressure lamp TQ 150, Hanau) at room temperature for 2.5 h; thereafter no more active chlorine was detectable with potassium iodide/ammonium acetate/starch. The reaction solution is finally poured into 150 ml ice-water; the precipitated product (11.2 g after drying in a vacuum) is filtered off and washed twice with cold dilute hydrochloric acid. Extraction of the combined aqueous phases for one day with ether affords (after drying in a vacuum) a further 0.6 g of the crude mixture of isomers.

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German version: Angew. Chem. *88*, 334 (1976)

CAS Registry numbers:
Hexanedioic acid, 124-04-9; heptanedioic acid, 111-16-0; octanedioic acid, 505-48-6; nonanedioic acid, 123-99-9; decanedioic acid, 111-20-6; dodecanedioic acid, 693-23-2; *N*-chlorodiisopropylamine, 24948-81-0

[1] *N. C. Deno, W. E. Billups, R. Fishbein, C. Pierson, R. Whalen,* and *J. C. Wyckoff*, J. Am. Chem. Soc. *93*, 438 (1971).
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Macrocyclic Peptides in Anionic Polymers of Amino Acid *N*-Carboxylic Anhydrides[**]

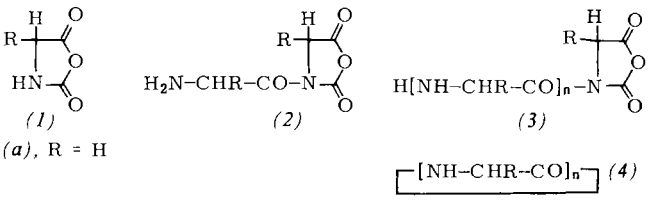
By *Manfred Rothe* and *Dietger Mühlhausen*[*]

Dedicated to Professor Werner Kern on the occasion of his 70th birthday

Amino acid *N*-carboxylic anhydrides (NCA) *(1)* can be polymerized anionically with tertiary bases or inorganic halides (LiCl, NaI)[1]. Reaction of NCA and the NCA anion according to a mechanism resembling that of the anionic lactam polymerization[2, 3] should give rise to initial formation of an *N*-aminoacyl-NCA *(2)*, which then undergoes reaction with further NCA molecules with loss of CO_2 to give poly-α-amino acids having a C-terminal NCA moiety *(3)*.

The isomerization of *(2a)* to 1-hydantoin acetic acid and the cyclization of *(3a)*, $n=5$, to cyclohexaglycyl *(4a)*, $n=6$, are known chain termination reactions.

We have found that glycine-NCA *(1a)* can also give rise to other macrocyclic peptides which could not be indentified previously because of their similarity to polyglycine (sparing solubility, high decomposition points, in part amorphous character). Extraction of anionic polymers with hot water and removal of linear peptides and inorganic salts with ion-



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

(a), R = H

(4)

exchangers afforded a ninhydrin-negative mixture of cyclopeptides which could be separated by gel-permeation chromatography on Merckogel PGM 2000 in water; the peaks were detected by differential refractometry.

Evaluation of the gel chromatograms presented difficulties in the case of cyclic glycine peptides, since the first members of the series up to cyclopentaglycyl deviate from normal chromatographic behavior—evidently owing to their conformations. Only from cyclohexaglycyl onwards is the dependence of the elution volume on log MW approximately linear. This could be demonstrated with ring peptide mixtures obtained by cyclization of linear oligoglycines at moderate concentrations using the phosphite method[4]. In each case the "monomeric" rings are accompanied by cyclic dimers, trimers, and tetramers, *i.e.* diglycine gives cyclotetra-, cyclohexa-, and cyclooctaglycyl along with glycine anhydride and triglycine gives cyclononaglycyl along with cyclohexaglycyl, while cycloocta- and cyclododecaglycyl or cyclodecaglycyl, respectively, are formed as higher ring oligomers from tetra- and pentaglycine.

Combination of the results so obtained together with molecular weight determinations enabled definite assignment of the peaks of all the cyclooligoglycyls mentioned.

Identification of the ring peptides obtained in the anionic polymerization of *(1a)* was accomplished by gel- and thin-layer chromatography and in particular by mass spectrometry (molecular peaks and fragmentation patterns) and comparison of the isolated crystalline products with authentic cyclopeptides synthesized from the linear oligoglycines and 2-chloro-1,3,2-benzodioxaphosphole (*o*-phenylene chlorophosphite) using the dilution technique[4] (cyclotetra-, cyclopenta-[5], cyclohexaglycyl: in each case colorless needles, m. p. (dec) >330 °C, >330 °C, and >350 °C, respectively; yields 35, 18 and 46 %, respectively]. In this way small amounts of cyclotetraglycyl ($m/e=328$) and the new compounds cycloheptaglycyl ($m/e=399$), cyclonona-, and cyclododecaglycyl could be detected in the NCA polymerization. The molecular peaks of the higher, unusually difficultly volatile cyclopeptides had hitherto not been detected; here the ring size is deduced from gel chromatograms. Cyclodi-, cyclotri-, and cyclopentaglycyl were not detected. The type and number of rings formed afford information about the previously largely unknown tendency to form many-membered cyclic peptides and about ring-chain equilibria in polypeptides.

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(1a), 2185-00-4; *(2a)*, 58673-11-3; *(3a)*, 58692-71-0; *(4a)*, 3785-17-9

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[**] Cyclic Peptides, Part 22. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and BASF (Ludwigshafen).—Part 21: *M. Rothe* and *W. Kreiss*, Angew. Chem. *85*, 1103 (1973); Angew. Chem. Int. Ed. Engl. *12*, 1012 (1973).

[1] *D. G. H. Ballard, C. H. Bamford,* and *F. J. Weymouth*, Nature *174*, 173 (1954); Proc. Roy. Soc. *A 227*, 155 (1955).
[2] *C. H. Bamford* and *H. Block* in *M. A. Stahman*: Polyamino Acids, Polypeptides, and Proteins. Wisconsin University Press, Madison 1962, p. 65; *M. Swarc*, Adv. Polym. Sci. *4*, 1 (1965).
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[5] *G. Lüdke*, Diplomarbeit, Universität Mainz 1964.

Triorganophosphane-dichloro- and -dibromo-germanediyl and -stannanediyl: Phosphane-Stabilized Ge^{II} and Sn^{II} Halides

By *Wolf-Walther du Mont, Brigitte Neudert, Gero Rudolph,* and *Herbert Schumann*[*]

Silylene-, germylene-, and stannylene-phosphoranes corresponding to methylenephosphoranes are hitherto unknown. Only some phosphane-germanediyls and -stannanediyls formally analogous to methylenephosphoranes have been reported[1,2]. We have found that triorganophosphane-dichloro- and -dibromogermanediyls *(2)* can be obtained by α-elimination reactions from trihalogermylphosphanes *(1)*[3]:

$$[(CH_3)_3C]_2PGeX_3 + R_3P \longrightarrow [(CH_3)_3C]_2PX + R_3PGeX_2$$

(1)

(2a), R = C_6H_5, X = Cl
(2b), R = $(CH_3)_3C$, X = Cl
(2c), R = C_6H_5, X = Br

The fact that this reaction proceeds under very mild conditions—at 20°C in benzene—and the considerable thermal stability of the phosphanedihalogermanediyls indicate a surprisingly high formation tendency of the P—Ge bond in *(2)*. Thus organophosphanes readily displace dioxane from $GeCl_2 \cdot$ dioxane, leading to compounds *(2)* in high yield [*(2a)*: 87%; *(2b)*: 95%]:

$$[GeCl_2 \cdot C_4H_8O_2] + R_3P \longrightarrow R_3PGeCl_2 + C_4H_8O_2$$

Tri-*tert*-butylphosphane even undergoes a corresponding reaction with tin dichloride and dibromide:

$$[(CH_3)_3C]_3P + SnX_2 \longrightarrow [(CH_3)_3C]_3PSnX_2$$

(3a), X = Cl
(3b), X = Br

The adducts *(2)* and *(3)* are obtained as colorless crystals which are moderately soluble in benzene and only sparingly soluble in pentane. The coordination of the phosphorus is shown by ^1H- and ^{31}P-NMR spectra (Table 1).

Formulation of the phosphane-dihalogermanediyls and -stannanediyls as base-stabilized "germylenes" and "stannylenes" *(A)* and not as germylene- and stannylenephosphoranes *(B)* is supported by the following properties of compounds *(2)* and *(3)*: hydrogen chloride immediately cleaves the P—Ge and P—Sn bonds in *(2b)* and *(3a)*, giving phosphonium

$R_3P{:}\rightarrow\ddot{E}X_2$ *(A)* $\qquad R_3P{=}EX_2$ *(B)*

salts of the type $R_3PH^+ECl_3^-$. Fast exchange reactions already occur at room temperature with an excess of phosphane. Thus mixtures of tri-*tert*-butylphosphane with *(2b)*, *(3a)*, or *(3b)* give ^{31}P-NMR spectra invariably showing only one signal whose chemical shift is the average between that for the phosphane [$\delta^{31}P = 62.5$ ppm] and that of its adducts with EX_2. The ^1H-NMR spectra contain only a doublet with "coupling constants" $^3J(^1H^{31}P)$ between 9.8 Hz [tri-*tert*-butylphosphane] and the values for *(2b)*, *(3a)*, or *(3b)* (cf. Table 1).

If the phosphorus in *(2a)* or *(2b)* possesses a further reactive function then dichlorogermanediyl can insert into that bond in a subsequent reaction step, *e.g.*:

$$[GeCl_2 \cdot C_4H_8O_2] + R_2PCl \xrightarrow[-C_4H_8O_2]{} R_2P(GeCl_2)Cl \longrightarrow R_2PGeCl_3$$

R = $C(CH_3)_3$ *(4)* *(1)*

The transformation *(4)*→*(1)* is the first example of germylene insertion into a phosphorus-halogen bond. It demonstrates that α-eliminations of trichlorogermylphosphanes can be reversible. Since the insertion reaction *(4)*→*(1)* is much slower than formation of *(4)* we have been able to identify di-*tert*-butylchlorophosphane-dichlorogermanediyl *(4)* by spectroscopy [$\delta^1H = 1.29$ ppm, $^3J(HP) = 13.6$ Hz; $\delta^{31}P = 127.1$ ppm; $\nu(PGeCl_2) = 330$ and 275 cm^{-1}] and thus confirm the electrophilic attack of the germylene on the phosphorus-chlorine bond.

Tri-tert-butylphosphane-dichlorostannanediyl (3a)

$[(CH_3)_3C]_3P$ (2.0 g, 10 mmol) is added to a suspension of $SnCl_2$ (2.1 g, 11 mmol) in benzene (50 ml). After 2 h, unreacted $SnCl_2$ is separated off and the solution evaporated to dryness under reduced pressure. The colorless residue is dried at 1 torr; yield 3.5 g (90%) of *(3a)*.

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(2a), 51812-24-9; *(2b)*, 58802-38-3; *(2c)*, 58802-39-4; *(3a)*, 58802-40-7; *(3b)*, 58802-41-8; *(4)*, 58802-42-9; $[(CH_3)_3C]_2PGeCl_3$, 55748-12-4; $[(CH_3)_3C]_2PGeBr_3$, 58802-29-2; Ph_3P, 603-35-0; $[GeCl_2 \cdot C_4H_8O_2]$, 15656-63-0; $SnCl_2$, 7772-99-8; $SnBr_2$, 10031-24-0; $[(CH_3)_3C]_2PCl$, 13716-10-4; ^{31}P, 7723-14-0; ^{119}Sn, 14314-35-3

Table 1. Properties of the compounds *(2)* and *(3)*.

Cpd. [a]	M.p. [°C] [b]	$\nu(PEX_2)$ [cm^{-1}]	$\delta^{31}P$ [ppm] [c]	$J(^1HCC^{31}P)$ [Hz]
(2a) [2]	145—175	328, 313, 300	− 3.9	—
(2b)	175—176 (dec.)	322, 298	+35.6	12.2
(2c)	175—178 (dec.)	242, 227, 205	− 8.2	—
(3a) [d]	98—100	290, 250	+49.3	12.35
(3b)	112—114	204, 192	+46.8	12.4

[a] Composition confirmed by elemental analysis.
[b] In sealed capillaries (Cu block).
[c] Varian XL 100 (40.5 MHz); positive values correspond to downfield shifts relative to 85% H_3PO_4.
[d] ^{119}Sn Mössbauer data: *I. S.* = 3.20 ± 0.06, *Q. S.* = 1.43 ± 0.12 mm/s ($Ba^{119}SnO_3$ standard).

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[1] *H. Schumann, H. Köpf,* and *M. Schmidt,* Z. Naturforsch. *19b*, 168 (1964); *R. B. King,* Inorg. Chem. *2*, 199 (1963).
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Novel Redox Reactions of Tri-*tert*-butylphosphane with Tetrahalides of Germanium and Tin

By *Wolf-Walther du Mont, Brigitte Neudert,* and *Herbert Schumann*[*]

In combination with a tetrahalomethane, tertiary phosphanes are versatile reagents in preparative chemistry. In the absence of substrates triphenylphosphane and CCl_4, for ex-

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ample, undergo a complicated redox reaction to give dichlorotriphenylphosphorane and (triphenylphosphoranediylchloromethyl)triphenylphosphonium chloride[1]. In contrast, the reaction of phosphanes with the tetrachlorides of silicon, germanium, tin, or titanium has hitherto only been found to yield 1:1 or 2:1 adducts.

We have disovered that tri-*tert*-butylphosphane *(1)*, of which complexes with transition metals in low oxidation states are known, does not form stable addition compounds with element(IV) tetrahalides. Instead, *(1)* is oxidized by the tetrahalides of germanium and tin in benzene solution to give tri-*tert*-butylhalophosphonium salts *(2)*[2].

$$[(CH_3)_3C]_3P + EX_4 \longrightarrow [(CH_3)_3C]_3PX^+EX_3^-$$

(1)

(2a), E = Ge, X = Cl
(2b), E = Ge, X = Br
(2c), E = Sn, X = Cl
(2d), E = Sn, X = Br

Compounds of type (2) have also been formulated for the reaction of phosphanes with tetrahalomethanes (E=C) as ion-pair intermediate but have so far defied detection. The halophosphonium salts *(2a)*—*(2d)* however, are stable compounds open to identification by analysis and spectroscopy. Nevertheless, on variation of the stoichiometry formation of *(2)* may be followed by secondary reactions. Thus the anions $SnCl_5^-$ and $SnCl_6^{2-}$ are formed from $SnCl_4$ and *(2c)*. In the presence of an excess of *(1)* the halophosphonium salts are accompanied by tri-*tert*-butylphosphane-dichloro- and -dibromogermanediyls and stannanediyls which are poorly soluble in benzene[3]:

$$[(CH_3)_3C]_3PX^+EX_3^- + [(CH_3)_3C]_3P \rightleftarrows$$

(2) *(1)*

$$[(CH_3)_3C]_3PX^+X^- + [(CH_3)_3C]_3PEX_2$$

(3a), X = Cl — *(4a)*, E = Ge, X = Cl
(3b), X = Br — *(4b)*, E = Ge, X = Br
(4c), E = Sn, X = Cl

The ionic character of compounds *(2a)*—*(2d)* and *(3)* was established by comparison of vibrational and NMR spectra and of their conductivity with those of tri-*tert*-butyldihalophosphoranes, which also exist in ionic form, and by independent preparation of the chlorophosphonium salts (*e.g. (2c)* from *(3a)* with $SnCl_2$)[4]. The IR spectra of the tri-*tert*-butylhalophosphonium ions display remarkable analogies with those of the isoelectronic tri-*tert*-butylhalosilanes[5]. Two to three stretching vibrations between 500 and 620 cm^{-1} are to be assigned to the inner molecular framework C_3PX (C_{3v}) undergoing coupled vibrations. In keeping with the positive charge and the electronegative substituents at phosphorus the ^{31}P-NMR signals appear at very low field, and variation of the anions expectedly effects slight changes (Table 1).

Table 1. Properties of tri-*tert*-butylhalophosphonium salts *(2)* and *(3)*.

Cpd. [a]	M.p. [°C] [b]	$\nu(C_3PX)$ [cm^{-1}]	$\delta^{31}P$ [ppm] [c]	$J(^1HCC^{31}P)$ [Hz]
(2a)	111—116 (dec.)	612, 548	121.9	17.45
(2b)	106—109 (dec.)	605, 571, 520	123.7	17.3
(2c)	149—153 (dec.)	618, 545	122.0	17.4
(2d)	134—138 (dec.)	610, 578, 525	124.8	17.8
(3a)	76—77 (dec.)	618, 548	122.7	17.3
(3b)	86—88 (dec.)	610, 575, 522	121.2	17.25
tBu_3PI_2 [2]	145—150 (dec.)	600, 562, 508	92.5	16.55

[a] Composition confirmed by elemental analysis.
[b] In sealed capillaries (Cu block).
[c] Varian XL 100 (40.5 MHz); positive values correspond to downfield shifts relative to 85% H_3PO_4, solutions in CH_2Cl_2/C_6D_6.

The relatively low sensitivity of the cations *(2)* and *(3)* to hydrolysis can be rationalized by stereochemical arguments. The fact that the tetrahalides of germanium and tin behave not only as Lewis acids but also as oxidizing agents towards bases such as R_3P warrants attention.

Tri-tert-butylchlorophosphonium trichlorogermanate(II) (2a):

Compound *(1)* (2.0 g, 10 mmol) is added dropwise to a stirred solution of $GeCl_4$ (2.14 g, 10 mmol) in benzene (20 ml). Two liquid phases appear and the mixture exhibits slight warming. The lower phase is separated and freed from solvent at 0.1 torr/50 °C. Compound *(2a)* (4 g, 95%) is obtained as colorless crystals. The conductivity of a 0.01 M solution of *(2a)* in CH_2Cl_2 is $0.41 \times 10^{-3}\ \Omega^{-1}\ cm^{-1}$.

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(1), 998-40-3; *(2a)*, 58832-61-4; *(2b)*, 58832-64-7; *(2c)*, 58832-65-8; *(2d)*, 58832-66-9; *(3a)*, 58816-81-2; *(3b)*, 58816-82-3; *(4a)*, 58802-38-3; *(4b)*, 58832-59-0; *(4c)*, 58802-40-7; *(4d)*, 58802-41-8; *t*-Bu_3PI_2, 58816-83-4; $GeCl_4$, 10038-98-9; $GeBr_4$, 13450-92-5; $SnCl_4$, 7646-78-8; $SnBr_4$, 7789-67-5; ^{31}P, 7723-14-0

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[3] *W.-W. du Mont, B. Neudert, G. Rudolph*, and *H. Schumann*, Angew. Chem. *88*, 303 (1976); Angew. Chem. Int. Ed. Engl. *15*, 308 (1976).
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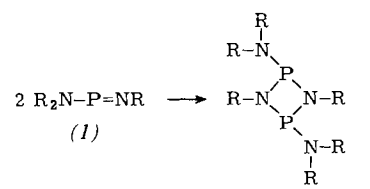
A Phosphorus(III) Derivative with Sterically Fixed Bis(trimethylsilyl)amino Groups[1]

By *Edgar Niecke, Wilhelm Flick*, and *Siegfried Pohl*[*]

According to present knowledge aminoiminophosphanes, phosphorus nitrogen ylides with a doubly coordinated P^{III} atom, are capable of existence in the monomeric form if there are sterically bulky substituents on the amine and imine nitrogens[2].

Especially interesting steric relations were to be expected if a [2+2]-cycloaddition product is observed besides a relatively stable monomer. We report here on the structural investigation of a compound of this type.

Pure bis(trimethylsilyl)aminotrimethylsilyliminophosphane *(1)* cyclizes slowly under inert gas at 25 °C to give 1,3-bis(trimethylsilyl)-*trans*-2,4-bis[bis(trimethylsilyl)amino]-1,3,2λ^3,4λ^3-diazadiphosphetidine *(2)*[3]. The crystalline product (m.p. 204—206 °C) can be obtained in pure form by separation from



the liquid monomer and subsequent repeated washing with small quantities of absolute cyclohexane.

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Composition and structure of *(2)* were proved by chemical analysis, mass spectrum, NMR data (^{31}P[4], ^{1}H, ^{29}Si) and by complete X-ray structure analysis.

The ^{1}H-NMR spectrum (10% solution in CH_2Cl_2; TMS int.[5], 25°C) shows three groups of signals with equal intensity—$\{^{31}P\}$: three singlets—which indicate sterically fixed bis(trimethylsilyl)amino groups.

$\delta(>NSiH) = -0.08$ ppm (t), $^{4}J_{HP} = 0.55$ Hz
$\delta(-N<^{SiCH}_{SiCH}) = -0.26$ ppm (t) [6], $|^{4}J_{HP} + {}^{6}J_{HP}| = 3.80$ Hz
$\delta(-N<^{SiCH}_{SiCH}) = -0.52$ ppm (s)

High-temperature ^{1}H-NMR measurements (10% solution in HMPT) do not show significant changes in the spectrum up to 240°C (decomposition) and indicate an extremely high barrier of rotation around the phosphorus-nitrogen bond ($\Delta G^{\ddagger}_{Tc} > 27$ kcal/mol).

In the ^{29}Si-$\{^{1}H\}$-FT NMR spectrum (10% solution in C_6F_6; TMS int.[5]) the different stereochemistry of the two trimethylsilyl groups on the exocyclic nitrogens becomes evident from two differentiated multiplets with pseudo triplet structure[7] as well as from strongly different absolute values of the ^{29}Si-^{31}P interactions.

$\delta(>NSi) = 0.6$ ppm (t), $^{2}J_{SiP} = 7.8$ Hz
$\delta(-N<^{Si}_{Si}) = 1.5$ ppm (t) [6], $|^{2}J_{SiP} + {}^{4}J_{SiP}| = 3.4$ Hz
$\delta(-N<^{Si}_{Si}) = -6.1$ ppm (t) [6], $|^{2}J_{SiP} + {}^{4}J_{SiP}| = 31.0$ Hz

The X-ray structure analysis substantiates the NMR spectroscopic findings. *(2)* crystallizes in the monoclinic space group $P2_1/c$ with $a = 9.370$, $b = 16.348$, $c = 12.985$ Å; $\beta = 119.87°$; $V = 1725$ Å^3; $Z = 2$. The refinement with the structure factors of 2877 observed reflections converged to an R value of 4.5%.

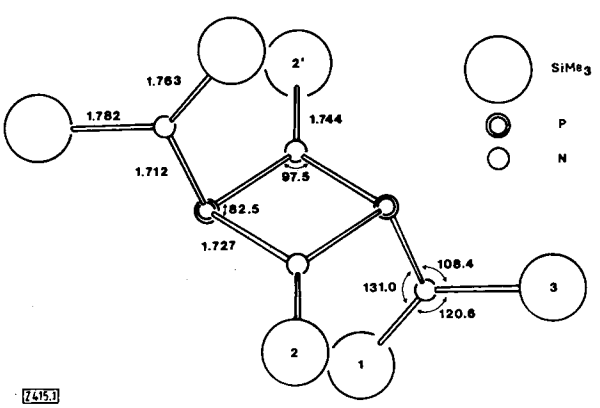

Fig. 1. Molecular structure of the diazadiphosphetidine *(2)*; bond lengths [Å] and bond angles [°].

In the crystal the molecule has C_i symmetry. Consequently, the P_2N_2 ring is exactly planar and the $(Me_3Si)_2N$ groups are *trans* to each other. The Si atoms bonded to the endocyclic nitrogen atoms are also in the plane of the ring. The bonding in the four-membered ring (Fig. 1) is similar to that in other known diaza-λ^3-diphosphetidines[7]. However, the two P—N—Si bond angles on the exocyclic N show an unusually high difference (108.4 *vs.* 131.0°). The abnormally high value of one of them is caused by steric hindrance and fixation of $SiR_{3(1)}$ between $SiR_{3(2)}$ and $SiR_{3(2')}$, the same hindrance leading to the high barrier of rotation within the free molecule in solution. This stereochemistry explains the unusually high difference of the J_{SiP} values in the $PNSi_2$ skeleton, the smaller bond angle belonging to the larger absolute value of the ^{29}Si-^{31}P coupling[8]. As a consequence, there is stronger interaction with the Si atom in ecliptic configuration to the "free" electron pair of the phosphorus atom; this is in agreement with investigations on aminophosphanes with restricted rotation[9].

The results indicate that in *(2)* the limit of steric strain by bulky substituents is evidently reached within the class of [2+2]-cycloaddition products of aminoiminophosphanes. This is in accord with the earlier observation that no cyclization ensues on replacing the trimethylsilyl groups in *(1)* by the sterically still more voluminous *tert*-butyl substituents[2].

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(1), 50732-21-3; *(2)*, 58802-30-5; ^{31}P, 7723-14-0; ^{29}Si, 14304-87-1

[1] Investigations on Phosphazenes with Coordination Numbers 2 and 3, Part 9. This work was supported by the Deutsche Forschungsgemeinschaft.—Part 8: *E. Niecke* and *W. Flick*, J. Organomet. Chem. *104*, C23 (1976).
[2] *E. Niecke* and *O. J. Scherer*, Nachr. Chem. Techn. *23*, 395 (1975); and literature cited therein.
[3] *Ca.* 10% in 2 months; the rate of conversion is increased by higher temperatures and addition of catalytic quantites of acyl halides.
[4] $\delta^{31}P = -225.9$ ppm (10% solution in C_6H_{12}, 85% H_3PO_4 ext.) [5].
[5] $\delta(^{1}H, ^{29}Si, ^{31}P) < 0$ is defined as lower field relative to the standard.
[6] Pseudo-triplet structure of spin system $(AX_n)_2$ ($A = {}^{31}P$, $X = {}^{1}H$ or ^{29}Si) results from $|J_{AA}| > |J_{AX} - J'_{AX}|$.
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Interaction of the Walsh Orbitals in Bicyclopropyl[1]

By *Peter Asmus* and *Martin Klessinger*[*]

The extent of conjugative interaction between the Walsh orbitals of bicyclopropyl has been the topic of numerous studies[2]. Sterically fixed bicyclopropyls, in which the first four PE bands can be assigned to the combinations ω_{as}^{-}, ω_{s}^{-}, ω_{s}^{+}, and ω_{as}^{+} of the Walsh orbitals of the two cyclopropane units[1,3], afford values for the interaction from which it is impossible to estimate to what extent they are modified relative to the values for unsubstituted bicyclopropyls by substituent effects and steric effects. That these effects can reach considerable magnitudes is apparent from the results obtained for the analogous *exo*-dimethylene compounds where $\beta \approx -1.90$ eV compares with the value of $\beta = -2.40$ eV for unsubstituted butadiene[4].

Investigation of unsubstituted bicyclopropyl by photoelectron spectroscopy is difficult because eight ionizations from combinations of the Walsh orbitals of the *trans*- ($\phi = 180°$) and *gauche*-conformation ($\phi = 35$—$40°$) present in a ratio of about 40:60 in the gas phase[5] are predicted to occur in the comparatively narrow range of *ca.* 9—11 eV. Nevertheless, we have now succeeded in analyzing the PE spectrum of unsubstituted bicyclopropyl[6] by comparison with the spectra of sterically fixed bicyclopropyls and the results of MINDO/2 calculations. In this way it can be demonstrated that the strongly conformationally dependent conjugative interaction of the Walsh orbitals measured by the orbital splitting in

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bicyclopropyl ($\Delta I_{as} = 2.3$—2.5 eV) is of approximately the same magnitude as the interaction of the orbitals of the double bonds in butadiene ($\Delta I = 2.45$ eV), while the substituent effects in the 1,1′-disubstituted sterically fixed bicyclopropyl derivatives considerably reduce this interaction.

It follows from the energies of the Walsh orbitals of unsubstituted bicyclopropyl and 1,1′-dimethylbicyclopropyl calculated as functions of the dihedral angle ϕ by the MINDO/2 method[7] (i) that in unsubstituted bicyclopropyl the splitting $\Delta I_{as} = I(\omega_{as}^{+}) - I(\omega_{as}^{-})$ should be somewhat larger for the *cis*-conformation than for the *trans*-conformation, (ii) that for dihedral angles between 0 and 80°, in keeping with the angular dependence of the resonance integral β, the splitting is given by the relation

$$\Delta I_{as} = \Delta I_{as}^{0} \cos\phi$$

and (iii) that in the *cis*-conformation alkyl substitution, as in the butadiene system, effects both a general destabilization of all orbitals and a reduction of ΔI_{as} by about 0.4 eV.

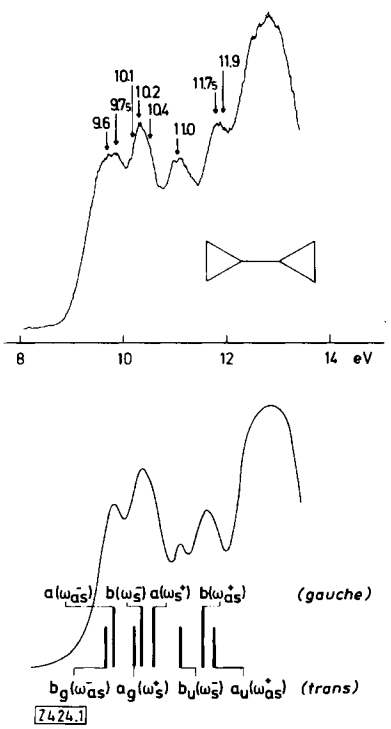

Fig. 1. PE spectrum of bicyclopropyl: above, recorded with a Perkin-Elmer PS 16 instrument (Xe/Ar calibration); below, calculated for *gauche/trans* ≈60:40.

In Figure 1 the spectrum predicted on the basis of MINDO/2 results and the assumption of Lorentz curves of 0.5 eV half-width for a mixture of conformers having the given composition is compared with the measured PE spectrum. Agreement is so good as to apparently justify the assignments given. These data yield a splitting of $\Delta I_{as}(trans) = 2.32$ eV for the *trans*-conformation of unsubstituted bicyclopropyl, corresponding to a HMO resonance integral $= -1.74$ eV, which fits very well into the series of values of $\beta = -2.45$ eV for *trans*-butadiene[8a] and $\beta = -2.1$ eV for the *trans*-form of vinylcyclopropane[8b]. With the aid of the cosine relation the value $\Delta I_{as}(cis) \approx 2.5$ eV is calculated from $\Delta I_{as}(gauche) = 2.00$ eV; the corresponding value of β is *ca.* -1.9 eV. Comparison with the sterically fixed 1,1′-disubstituted bicyclopropyls shows that, as for the *exo*-dimethylene compounds[9], the magnitude of β is reduced by a total amount of about 0.45 eV by the inductive effect of the substituents and by a lengthening of the central CC bond. As in the case of substituted butadienes[8a], a perturbational treatment of the substituent effect accordingly fails to give consistent results[10].

It is striking that in contrast to butadiene the interaction energies $H_{RS} = c_{\rho}^{R} c_{\sigma}^{S} \beta_{\rho\sigma}$ determining the orbital splitting are different for the *cis*- and *trans*-forms of bicyclopropyl: $H_{RS}(cis) = -1.25$ eV and $H_{RS}(trans) = -1.16$ eV (for comparison: $H_{RS} = -1.23$ eV for butadiene).

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revised: February 19, 1976 [Z 424 IE]
German version: Angew. Chem. *88*, 343 (1976)

CAS Registry number:
Bicyclopropyl, 5685-46-1

[1] Photoelectron Spectra of Organic Compounds, Part 10.—Part 9: *P. Asmus* and *M. Klessinger*, Justus Liebigs Ann. Chem. *1975*, 2169.
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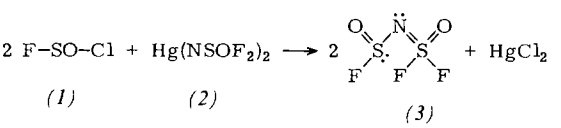
[9] *P. Hemmersbach*, Diplomarbeit, Universität Münster 1975.
[10] Values of $\beta = -1.64$ and -1.73 eV [3] for the *cis*-form are obtained with 1,1′- and 2,2′-disubstituted derivatives, respectively, as compared with the above value of $\beta = -1.9$ eV.

Fluorosulfinylimidosulfur Oxide Difluoride[**]

By *Hans-Joachim Krannich* and *Wolfgang Sundermeyer*[*]

Sulfinyl pseudohalides tend to disproportionate into the corresponding sulfenyl and sulfonyl compounds, which are in turn frequently unstable[1,2]. In contrast, halosulfinyl pseudohalides appear to resist decomposition of this kind[3]. From the hitherto unknown series of the halosulfinylimidosulfur oxide difluorides, X—SO(NSOF$_2$), we have now prepared the fluorine compound *(3)*, X=F, as the first representative by reaction of sulfinyl chloride fluoride *(1)*[4] with mercury bis(imidosulfur oxide difluoride) *(2)*[5].



In a vacuum system, compound *(1)* (12 g) is condensed onto *(2)* (6.5 g) and the suspension stirred for 1 h at room temperature. The volatile components are again condensed onto the same quantity of *(2)* and the mixture once more allowed to react for 1 h. Distillation of the volatile components drawn off affords *(3)* (8.5 g, 78 %) as a water-clear liquid boiling at 64 °C.

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are grateful to Priv.-Doz. Dr. *K. Seppelt* for his help in interpreting the NMR spectrum.

The existence of *(3)* is confirmed by elemental analysis and the mass spectrum (70 eV): $m/e = 167$ molecular ion (rel. int. 36.7 %), 148 OS—$NSOF_2$ (9.8), 100 $NSOF_2$ (1.7), 86 SOF_2 (5), 70 SF_2? (3.3), 67 SOF (100), 65 NSF (1.9), 62 NSO (5.3), 51 SF (3.1), 48 SO (10.5), 46 NS (9.1), 32 S (2.5), and 30? (6.6).—The IR spectrum contains bands at 1425 (vs, νSO, $NSOF_2$), 1271 (m, νSO), 1182 (vs, νNS), 872 (vs, νSF), 735 (w), 698 (w), 655 (w), 490 (m), and 450 cm^{-1} (m).

Compound *(3)* gives an unusual ^{19}F-NMR spectrum. Instead of the expected doublet and triplet it contains a quartet at −57.98 ppm (SOF) and an octet at −52.48 ppm (ABX type), *i. e.* the fluorine atoms of the $NSOF_2$ group are diastereotopic and couple with each other as well as with the fluorine atom attached to the unsymmetrically substituted sulfur atom of the sulfinyl group: $\delta_X = -57.98$, $\delta_A = -52.54$, $\delta_B = -52.43$ ppm; $J_{AB} = 193.6$, $J_{AX} = 8.3$, $J_{BX} = 8.3$ Hz (F_X—SO—$NSOF_AF_B$).

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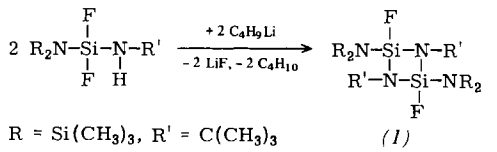
German version: Angew. Chem. *88*, 338 (1976)

CAS Registry numbers:
(1), 14177-25-4; *(2)*, 31618-64-1; *(3)*, 58816-64-1

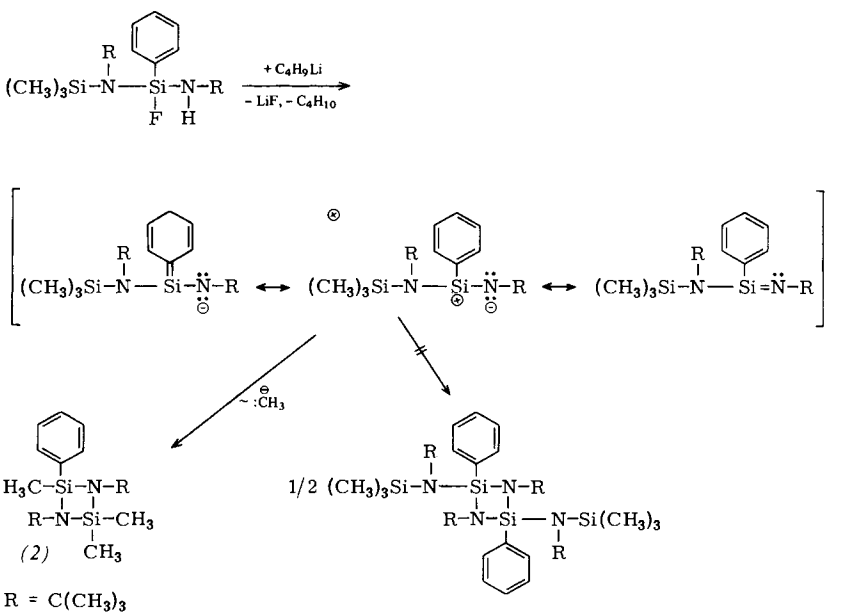
[1] *P. W. Schenk* and *H. Bloching*, Chem. Ber. *92*, 2333 (1959).
[2] *W. Lidy*, Dissertation, Universität Heidelberg 1974.
[3] *H.-J. Krannich* and *W. Sundermeyer*, Angew. Chem. *88*, 88 (1976); Angew. Chem. Int. Ed. Engl. *15*, 110 (1976).
[4] *H. S. Booth* and *F. C. Mericola*, J. Am. Chem. Soc. *62*, 640 (1940).
[5] *K. Seppelt* and *W. Sundermeyer*, Angew. Chem. *82*, 931 (1970); Angew. Chem. Int. Ed. Engl. *9*, 905 (1970).



However, if a fluorine atom of *tert*-butylaminodifluorosilane is replaced by an aryl group[4] the reaction takes an unusual course: The product obtained is an unsymmetrically substituted cyclic system whose formation can be attributed to a nucleophilic 1,3-rearrangement at silicon (comparable with the known methyl shift in a carbon skeleton) and also be regarded as evidence for generation of a silicon ylide. The absence of oligomerization products of type *(1)* shows the steric influence of the nitrogen atoms alone to provide insufficient stabilization of such a species with silicon having the coordination number 3[5]. Instead, the expected extremely high reactivity of this intermediate leads to intramolecular nucleophilic substitution with migration of a methanide ion and ring closure to give *(2)*.

Procedure:

C_4H_9Li (0.11 mol, as 15 % solution in hexane) is added dropwise at room temperature to monoalkylaminofluorosilane (0.1 mol) with stirring. An exothermic reaction ensues, liberating lithium fluoride and butane, which is condensed in a cold trap. After boiling for 12 h the hexane is distilled of *in vacuo* and the residue vacuum sublimed.



Nucleophilic 1,3-Rearrangement at Silicon—Indirect Evidence for a Silicon-Nitrogen Ylide[**]

By *Uwe Klingebiel* and *Anton Meller*[*]

Apart from bimolecular ring closure reactions of halosilanes with amines or ammonia[1], stable monoalkylaminofluorosilanes[2] can be cyclized directly by the action of *n*-butyllithium[3], the reaction mechanism being interpretable in intramolecular or intermolecular terms:

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

The composition of the new compounds was confirmed by elemental analysis and vibrational spectroscopy:

1,3-Di-tert-butyl-2,4-di[bis(trimethylsilyl)amino]-2,4-difluorocyclodisilazane (1)

Yield 65 %; m.p. 204 °C; MS (70 eV): $m/e = 556$ (rel. int. 3 %, M^+); ^{1}H-NMR (in CH_2Cl_2, TMS int. standard): −0.15, −0.31 [$(Me_3Si)_2N$, *cis/trans* isomers; $J_{HF} = 0.9$ Hz] −1.29 ppm (tBu); ^{19}F-NMR (with C_6F_6 as internal standard): −56.25, −57.33 ppm.

1,3-Di-tert-butyl-2,2,4-trimethyl-4-phenylcyclodisilazane (2)

Yield 88 %; m.p. 57 °C; MS (70 eV): $m/e = 320$ (rel. int. 3 %, M^+); ^{1}H-NMR (in CH_2Cl_2, TMS int. standard): −0.38,

−0.47 (Me_2Si), −0.68 (MeSi), −1.04 (tBu), −7.52 ppm (Ph); ^{29}Si-NMR (in C_6F_6, TMS int. standard; ^{1}H-noise decoupled): −1.2 (Me_2Si), +11.5 ppm (MeSi).

Received: January 21, 1976;
revised: February 9, 1976 [Z 420 IE]
German version: Angew. Chem. 88, 307 (1976)

CAS Registry numbers:
(1), 58816-84-5; (2), 58816-85-6; $[(CH_3)_3Si]_2NSiF_2NHC(CH_3)_3$, 58816-86-7; $(CH_3)_3SiN[C(CH_3)_3]SiF(Ph)NHC(CH_3)_3$, 58816-87-8

[1] W. Fink, Angew. Chem. 78, 803 (1966); Angew. Chem. Int. Ed. Engl. 5, 760 (1966); U. Wannagat and M. Schlingmann, Z. Anorg. Allg. Chem. 406, 7 (1974).
[2] U. Klingebiel, D. Fischer, and A. Meller, Monatsh. Chem. 106, 459 (1975).
[3] U. Klingebiel and A. Meller, Chem. Ber., in press.
[4] U. Kleingebiel and A. Meller, to be published.
[5] P. Jutzi, Angew. Chem. 87, 269 (1975); Angew. Chem. Int. Ed. Engl. 14, 232 (1975).

Synthesis of an *N*-Lithioaminofluorosilane[**]

By *Uwe Klingebiel* and *Anton Meller*[*]

Although fluorosilanes differ from other halosilanes in their reaction with amines, they nevertheless undergo analogous substitution reactions with the lithium salts of amines[1]. The action of *n*-butyllithium on monoalkylaminofluorosilanes leads *via* loss of lithium fluoride and butane to ring closures of various kinds[2]. With the aim of suppressing such cyclizations and of stabilizing an intermediate silicenium ylide[2] we have prepared the aminofluorosilane *(1)*, exhibiting optimal steric shielding, by reaction of di-*tert*-butyldifluorosilane[3] with lithium *tert*-butylamide:

$$[(CH_3)_3C]_2SiF_2 \xrightarrow[-\,LiF]{+\,LiNHC(CH_3)_3} [(CH_3)_3C]_2\underset{F}{\overset{}{Si}}-\underset{H}{\overset{}{N}}-C(CH_3)_3 \qquad (1)$$

As expected, *(1)* shows little tendency to react with *n*-butyllithium relative to other aminofluorosilanes. Evolution of butane is only observed on raising the temperature, whereupon a colorless solid crystallizes which proves to be the first aminofluorosilane lithiated on the nitrogen atom *(2)*:

$$(1) \xrightarrow[-\,C_4H_{10}]{+\,C_4H_9Li} [(CH_3)_3C]_2\underset{F}{\overset{}{Si}}-\underset{Li}{\overset{}{N}}-C(CH_3)_3 \qquad (2)$$

The ready hydrolysis of *(2)* and its solubility in organic solvents correspond to those of other lithium amides. However, the thermal stability of this compound is remarkable: it only sublimes above 125 °C with partial decomposition and formation of polymeric products. The unusually large upfield shifts of the ^{19}F-NMR signals of *(1)* and *(2)* is explained by the electron pressure of the *tert*-butyl groups. Molecular weight determination and the spatial structure of the compound rule out association of *(2)*. Elemental analysis and vibrational spectra support the structures given.

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

Procedure:

C_4H_9Li (0.1 mol, 15 % solution in hexane) is added dropwise at room temperature under N_2 to compound *(1)* (0.1 mol) with stirring. Warming of the reaction mixture to *ca.* 50 °C effects liberation of butane which is condensed in a cold trap. The metalation is driven to completion by boiling for another 2 h. The product *(2)* can be purified by recrystallization from hexane or by sublimation at 120 °C/0.1 torr.

Di-tert-butyl(tert-butylamino)fluorosilane (1)

Yield 85 %; b.p. 80 °C/8 torr; MS (70 eV): *m/e* = 233 (rel. int. 1 %, M^+); ^{1}H-NMR (in C_6H_6, TMS int. standard): −1.05 (tBuSi; J_{HF} = 1.0 Hz), −1.20 ppm (tBuN; J_{HF} = 0.8 Hz); ^{19}F-NMR (in C_6H_6, $CFCl_3$ ext. standard): +168.09 ppm, J_{HNF} = 8.0 Hz; ^{29}Si-NMR (in C_6F_6, TMS int. standard; ^{1}H-noise decoupled): −0.7 ppm, J_{SiF} = 300.3 Hz.

N-Lithiodi-tert-butyl(tert-butylamino)fluorosilane (2)

Yield 80 %; m.p. >125 °C (dec.); MW (osmometric in $CHCl_3$): 252; ^{1}H-NMR (in C_6H_6, TMS int. standard): −1.20 (tBuSi), −1.23 ppm (tBuN); ^{19}F-NMR (in C_6H_6, $CFCl_3$ ext. standard): +162.41 ppm.

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German version: Angew. Chem. 88, 304 (1976)

CAS Registry numbers:
(1), 58802-36-1; (2), 58802-37-2; $[(CH_3)_3C]_2SiF_2$, 558-63-4; $LiNHC(CH_3)_3$, 37828-54-9; ^{29}Si, 14304-87-1

[1] U. Klingebiel and A. Meller, Chem. Ber., in press.
[2] U. Klingebiel and A. Meller, Angew. Chem. 88, 307 (1976); Angew. Chem. Int. Ed. Engl. 15, 312 (1976).
[3] M. Weidenbruch and W. Peter, Angew. Chem. 87, 670 (1975); Angew. Chem. Int. Ed. Engl. 14, 642 (1975).

Nucleophilic Aminoalkylation. Lithiated *N,N*-Dimethylthiopivalamide[1][**]

By *Dieter Seebach* and *Winfried Lubosch*[*]

In the search for activating groups X in *(1)* which permit metalation to *(2)* (CH acidification of amines) several derivatives have been examined. The group X should be such that it is neither attacked by the deprotonating reagent employed (as with X = CN[2], CHO[3], and CHS[4]) nor undergo facile departure from *(2)* as LiX (as with X = NO_2[5] and Tosyl[2]); nor should self-condensation with the precursor *(1)* occur on generation of *(2)* (as with X = benzoyl[6] and $\overset{\oplus}{C}(C_6H_5)_2$[7]),

$$\left[\begin{array}{c} X \\ | \\ R-N-CH_3 \end{array} \longleftrightarrow \begin{array}{c} X^{\ominus} \\ \| \\ R-\overset{\oplus}{N}-CH_3 \end{array}\right] \xrightarrow{\text{Base}} \begin{array}{c} X \\ | \\ R-N-CH_2Li \end{array}$$

(1) (2)

(a), X = NO; (b), X = $(CH_3)_3C-\overset{S}{\overset{\|}{C}}$

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and finally the extent of acidification by X should be sufficient to obviate any need for additional stabilization of the carbanionoid center of *(2)* (as with $X = POX_2$[8]). So far only the nitrosamines *(1a)* have proved to be aminomethylation agents of broad scope[2].

We have now found the thiopivaloyl group to be another substituent permitting quantitative metalation to give stable derivatives (up to −50 °C) of type *(2)*. Thus conversion of *(3)* into the organolithium compound *(4)* can be accomplished under the conditions given in the reaction scheme. Reaction of *(4)* with alkyl halides and carbonyl compounds proceeds *via* C—C linkage to form the products *(5)* (Table 1). Alkylations are more successful than hydroxyalkylations;

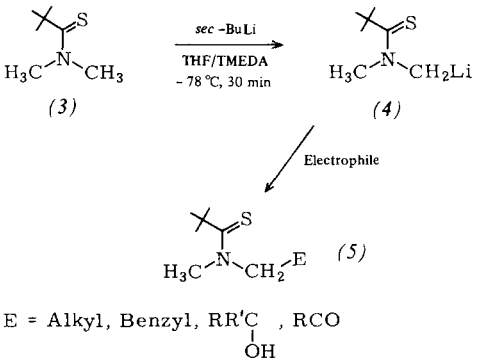
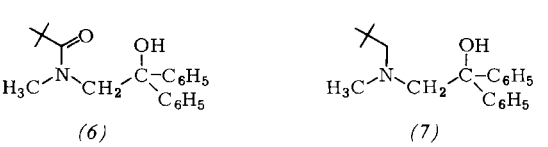


Table 1. Reactions of *(4)* with electrophiles to form products of type *(5)* [a, b].

Electrophile	Yield % spectr. [c]	pure [b]	^{1}H-NMR [d] δ [ppm]
CH_3I	95	80	3.97 (q)
n-$C_5H_{11}I$	91	82	3.86 (br. t)
n-$C_{10}H_{21}Br$	80	79	3.87 (br. t)
$C_6H_5CH_2Br$	48	44	4.08 (m)
C_6H_5CHO	85	70	4.18 (m)
$(C_6H_5)_2CO$	78	63	5.16 (s)
$(CH_3)_2CH$—CHO	80	23	3.73—4.02 (m)
Cyclohexanone	27	17	4.24 (s)
$CH_3CON(CH_3)_2$	56	33	4.71 (s)

[a] NMR data not listed as well as other spectroscopic data (*e.g.* two broad thioamide bands at 1330—1420 and 1450—1510 cm^{-1}) and elemental analyses (within 0.3 %) all accord with the expected structures.
[b] Apart from the adducts with benzaldehyde (m.p. 105 °C), benzophenone (m.p. 150 °C), and cyclohexanone (m.p. 104.5 °C) compounds *(5)* are oils which were purified by chromatography.
[c] From weight of crude product and NMR comparison with analytically pure material.
[d] The α-N-CH_2 signal is given. The *tert*-butyl group appears between 1.38 and 1.46, the methyl group between 3.2 and 3.5 ppm (both singlets). Solvent CCl_4 or $CDCl_3$.

this contrasts with the situation in the case of lithiated nitrosamines which can be described as typical carbonylophiles[2].



The thioamides *(5)* can be smoothly transformed into amides by alkaline H_2O_2[9], as we have demonstrated by preparing compound *(6)* (93 %, m.p. 95.5 °C). Neopentylamines are accessible from *(5)* by desulfuration with $LiAlH_4$[4b,10] (example: *(7)*; 88 %; m.p. 84.5 °C).

Received: March 23, 1976 [Z 432 IE]
German version: Angew. Chem. *88*, 339 (1976)

CAS Registry numbers:
(3), 25530-28-3; *(4)*, 58832-32-9; *(6)*, 58832-33-0; *(7)*, 58832-34-1
Table 1. Electrophiles (from top to bottom):
74-88-4; 628-17-1; 112-29-8; 100-39-0; 100-52-7; 199-61-9; 78-84-2; 108-94-1; 127-19-5
Table 1. *(5)* (from top to bottom):
58856-07-8; 58832-24-9; 58832-25-0; 58832-26-1; 58832-27-2; 58832-28-3; 58832-29-4; 58832-30-7; 58832-31-8

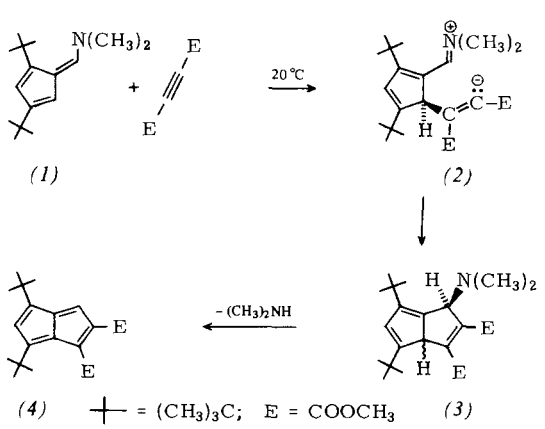
[1] Part of the projected Thesis by *W. L.*, Universität Giessen.
[2] *D. Seebach* and *D. Enders*, Angew. Chem. *87*, 1 (1975); Angew. Chem. Int. Ed. Engl. *87*, 15 (1975); *D. Enders*, Thesis, Universität Giessen 1974.
[3] *B. Bánhidai* and *U. Schöllkopf*, Angew. Chem. *85*, 861 (1973); Angew. Chem. Int. Ed. Engl. *85*, 836 (1973); *R. R. Fraser* and *P. R. Hubert*, Can. J. Chem. *52*, 185 (1974).
[4] a) *D. Enders* and *D. Seebach*, Angew. Chem. *85*, 1104 (1973); Angew. Chem. Int. Ed. Engl. *85*, 1014 (1973); b) *D. Seebach*, *W. Lubosch*, and *D. Enders*, Chem. Ber., in press.
[5] *R. Dach*, unpublished experiments, Universität Giessen (1974/75).
[6] *P. Beak* and *R. Farney*, J. Am. Chem. Soc. *95*, 4771 (1973).
[7] *H. Böhme* and *P. Plappert*, Chem. Ber. *108*, 2827 (1975).
[8] *P. Savignac et al.*, C. R. Acad. Sci. *C279*, 609 (1974); Tetrahedron Lett. *1974*, 2651; J. Organomet. Chem. *57*, C47 (1973); Tetrahedron *31*, 877 (1975).
[9] *H. Vorbrüggen* and *P. Strehlke*, Chem. Ber. *106*, 3039 (1973).
[10] *M. W. Cronyn* and *J. E. Goodrich*, J. Am. Chem. Soc. *74*, 3936 (1952).

[6+2] Cycloadditions of Pentafulvene. A Facile Pentalene Synthesis[**]

By *Klaus Hafner* and *Minoru Suda*[*]

The hitherto known syntheses of pentalene and its derivatives require several reaction steps and frequently the isolation of rather unstable intermediates[1]. We have found that the [6+2]cycloaddition[2] of 6-dimethylaminofulvenes with electron-deficient acetylene derivatives offers a facile synthesis of pentalenes which can be carried out as a "one batch procedure" at 20 °C.

While 6-dimethylaminofulvene undergoes a Michael addition with dimethyl acetylenedicarboxylate at 20 °C in benzene[3], 1,3-di-*tert*-butyl-6-dimethylaminofulvene *(1)*[4] combines with the alkyne under the same reaction conditions, presumably *via* the dipolar intermediate *(2)* and its cyclization product *(3)*, to give the thermally- and air-stable dimethyl 4,6-di-*tert*-butylpentalene-1,2-dicarboxylate *(4)*.



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

The electronic spectrum of *(4)* (in *n*-hexane) resembles that of 1,3,5-tri-*tert*-butylpentalene[1], except for a bathochromic shift of the longest wavelength maximum by 70 nm [$\lambda_{max}=259$ ($\log\varepsilon=4.29$), 357 (3.71), and 668 nm (2.36)] due to the ester groups. The 60-MHz ^{1}H-NMR spectrum of *(4)* (in $CDCl_3$), which provides proof of structure, consists of six singlets, of which two are assigned to the two ring protons [$\tau=3.85$ (H-3) and 5.07 (H-5)], two to the ester methyl protons ($\tau=6.24$ and 6.36), and two to the *tert*-butyl protons ($\tau=8.96$ and 9.02). The relatively high upfield shift of the H-5 signal indicates the presence of a paramagnetic ring current in *(4)*. The ^{13}C-NMR spectrum of *(4)* (in $CDCl_3$) shows one signal each for the eight ring C atoms at $\delta=129.3$ (C-5), 134.7 (C-3), 135.1, 135.9 (C-1, C-2), 141.6, 143.7 (C-6a, C-3a), 161.7 and 162.9 (C-4, C-6), four signals for the *tert*-butyl C atoms at $\delta=27.9$ and 28.6 (CH_3), 33.0 and 34.9 (quat. C), and four for the ester C atoms at $\delta=51.3$ and 51.9 (CH_3O) and 167.4 and 173.0 (C=O). In contrast to pentalene and its simple alkyl derivatives[5], compound *(4)*, like 1,3,5-tri-*tert*-butylpentalene[1], shows no tendency to dimerize even at elevated temperatures[6].

(5) *(6)*

┼ = $(CH_3)_3C$; R = $COOCH_3$, CHO

Treatment of *(1)* with methyl propiolate or propiolaldehyde affords a *ca.* 40 % yield of the pentalene derivatives *(5)* which are in equilibrium with their dimers *(6)* at room temperature. A study of this equilibrium reaction is in progress.

Dimethyl 4,6-di-tert-butylpentalene-1,2-dicarboxylate (4)

To a solution of *(1)* (1.17 g, 5.0 mmol) in anhydrous benzene (50 mol) is added dimethyl acetylenedicarboxylate (1.50 g, 10.6 mmol) at room temperature. After 2 h, the solvent is removed from the green reaction solution *in vacuo* and the residue chromatographed over silica gel (Kieselgel 60, Merck) with *n*-hexane/ether (10:1). The eluate of the leading blue zone is extensively concentrated at room temperature *in vacuo* and the residue cooled to −70 °C. The fine blue crystals precipitated are filtered off. Compound *(4)* (0.73 g, 44 %) is isolated analytically pure; it is obtained as blue plates, m.p. 120—121 °C, by recrystallization from *n*-hexane.

Received: March 4, 1976 [Z 434 IE]
German version: Angew. Chem. *88*, 341 (1976)

CAS Registry numbers:
(1), 58832-18-1; *(4)*, 58832-19-2; dimethyl acetylenedicarboxylate, 762-42-5

[1] *K. Hafner* and *H. U. Süss*, Angew. Chem. *85*, 626 (1973); Angew. Chem. Int. Ed. Engl. *12*, 575 (1973); and references cited therein.

[2] A [6+2] cycloaddition of 6,6-dicyclopropylfulvene with tetracyanoethylene is reported by *A. Cornelis* and *P. Laszlo*, J. Am. Chem. Soc. *97*, 244 (1975). [6+4] cycloadditions of 6-aminofulvenes: *M. Sato*, *S. Ebine*, and *J. Tsunetsugu*, Tetrahedron Lett. *1974*, 2769; *T. Sasaki*, *K. Kanematsu*, and *K. Kataoka*, J. Org. Chem. *40*, 1201 (1975); cf. also *K. N. Houk*, Acc. Chem. Res. *8*, 361 (1975).

[3] *F. Schmidt*, Dissertation, Technische Hochschule Darmstadt 1971; cf. also *K. Hafner*, Pure Appl. Chem. Suppl. Vol. *2*, 1 (1971).

[4] Prepared by analogy with 6-dimethylaminofulvene (Org. Synth. *47*, 52 (1967)) from lithium 1,3-di-*tert*-butylcyclopentadienide and methoxymethylenedimethylammonium monomethyl sulfate in ether/dichloromethane (1:1) at 0 °C: yellow needles of m.p. 116—118 °C; yield 51 % (*H. U. Süss*, Dissertation, Technische Hochschule Darmstadt 1976).

[5] *K. Hafner*, *R. Dönges*, *E. Goedecke*, and *R. Kaiser*, Angew. Chem. *85*, 362 (1973); Angew. Chem. Int. Ed. Engl. *12*, 337 (1973).

[6] An X-ray structural analysis of *(4)* is being performed by Prof. *H. J. Lindner* (Darmstadt).

(Dichloromethylene)triphenylphosphorane

By *Rolf Appel*, *Fritz Knoll*, and *Harald Veltmann*[*]

(Dichloromethylene)triphenylphosphorane *(3)* is obtained from triphenylphosphane and dichlorocarbene, which is generated from chloroform and potassium *tert*-butoxide[1] during the reaction. On reaction of triphenylphosphane with carbon tetrachloride the species *(3)* also arises as a short-lived intermediate[2], which resists isolation—just as in the preparation according to ref. [1]—and can only be detected by Wittig reaction with carbonyl compounds.

The first indications of a possible isolation were provided by attempted preparations of *(3)* by dechlorination of (trichloromethyl)triphenylphosphonium chloride *(1)* and dehydrochlorination of (dichloromethyl)triphenylphosphonium chloride *(5)* with an excess of bis(triphenylphosphoranylidene)methane according to equations (a) and (b), respectively[3].

$$\underset{(1)}{[Ph_3P{-}CCl_3]^{\oplus}\,Cl^{\ominus}} + \underset{(2)}{C(=PPh_3)_2} \longrightarrow \quad (a)$$

$$\underset{(3)}{Ph_3P{=}CCl_2} + \underset{(4)}{[Ph_3P{=}CCl{=}PPh_3]^{\oplus}\,Cl^{\ominus}}$$

$$\underset{(5)}{[Ph_3P{-}CHCl_2]^{\oplus}\,Cl^{\ominus}} + \underset{(2)}{C(=PPh_3)_2} \longrightarrow \quad (b)$$

$$\underset{(3)}{Ph_3P{=}CCl_2} + \underset{(6)}{[Ph_3P{=}CH{=}PPh_3]^{\oplus}\,Cl^{\ominus}}$$

During the reactions, which were performed in acetonitrile and dichloromethane, respectively, a singlet appeared in the ^{31}P-NMR spectrum (85 % H_3PO_4 as external standard) at −21.6 ppm which was not observed in any of the other preparations; it disappeared immediately upon addition of benzaldehyde. Thereafter triphenylphosphane oxide and β,β-dichlorostyrene could be detected.

This signal also gradually disappears in the absence of benzaldehyde, thus suggesting a deprotonation reaction of the ylide *(3)* with solvents. In order to record the ^{13}C-NMR spectrum the salt *(5)* bearing a ^{13}C label at the alkyl carbon atom was therefore treated with *(2)* in a deuteriobenzene suspension. The signal of the ylidic C atom which is split into a doublet by phosphorus coupling is seen at $\delta=-73.9$ ppm ($J_{P,^{13}C}=72.3$ Hz; minus sign indicates downfield shift). It was established by ^{13}C-NMR spectroscopy that hydrolysis of *(3)* affords only dichloromethane and triphenylphosphane oxide (TMS as internal standard).

Preparative scale isolation of the pure salt-free ylide *(3)* synthesized according to eq. (b) depends crucially upon the use of an aprotic solvent with which the strongly basic ylide is unable to form a corresponding acid-base pair. A suitable solvent system proved to be a mixture of chlorobenzene and toluene in which *(3)* displays adequate solubility. On removal of the solvent it remains behind as a yellow substance decomposing between 115 and 122 °C, which can be stored for several days. In contrast, solutions of *(3)* can only be stored for limited periods; they turn darker and darker while depositing a coating on the wall of the vessel. Apart from the ^{13}C-NMR spectrum, elemental analysis and cryoscopic molecular mass

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determination (calc. 345.2, exp. 335) confirm the existence and the monomeric structure of *(3)*. The mass spectrum contains the molecular peak ($m/e = 344$), accompanied by satellites due to the two chlorine atoms, at an ionization voltage of 13 eV.

Dehydrochlorination of (chloromethyl)triphenylphosphonium chloride *(7)* with an excess of *(2)* affords the (chloromethylene)phosphorane *(8)* whose ^{31}P-NMR signal is observed at -16.9 ppm. In contrast, the reaction according to eq. (d) is found on monitoring by ^{31}P-NMR spectroscopy to lead merely to a broadening of the signals of the starting compounds, which is probably attributable to comparable basicities of the two ylide systems coupled with a fast proton exchange.

$$\underset{(7)}{[Ph_3P{-}CH_2Cl]^{\oplus}\,Cl^{\ominus}} + \underset{}{(2)} \longrightarrow \underset{(8)}{Ph_3P{=}CHCl} + \underset{}{(6)} \qquad (c)$$

$$\underset{(9)}{[Ph_3P{-}CH_3]^{\oplus}\,Cl^{\ominus}} + \underset{}{(2)} \rightleftharpoons \underset{(10)}{Ph_3P{=}CH_2} + \underset{}{(6)} \qquad (d)$$

(Dichloromethylene)triphenylphosphorane (3)

Compounds *(5)*[4] (3.81 g, 0.01 mol) and *(2)*[5] (6.7 g, 0.0125 mol) are stirred together at room temperature for 6 h in chlorobenzene (10 ml) and toluene (15 ml). After filtration (glass frit) and washing (3×10 ml of toluene) of the residue consisting of *(6)* and excess *(2)* the clear filtrate is gently evaporated to dryness in a vacuum. Compound *(3)* (1.9 g, 55 %) is obtained as a yellow powder which can be redissolved as the monomer in toluene.

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CAS Registry numbers:
(2), 7533-52-0; *(3)*, 6779-08-4; *(5)*, 57212-38-1; *(6)*, 58513-98-7; *(7)*, 5293-84-5; *(8)*, 29949-92-6; *(9)*, 1031-15-8; *(10)*, 3487-44-3; ^{31}P, 7723-14-0

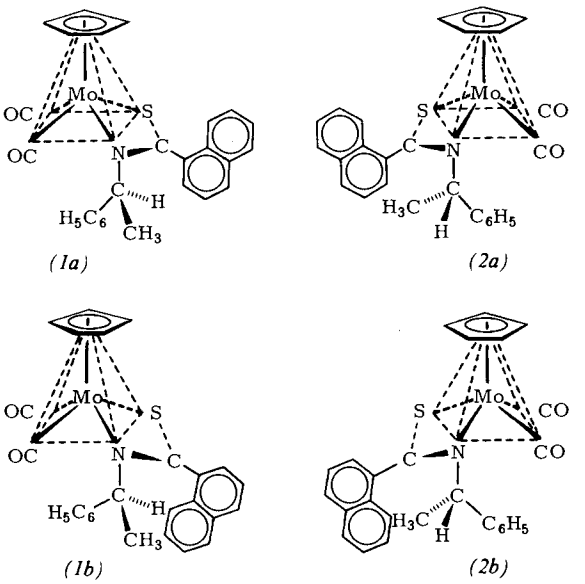
[1] *A. J. Speziale, G. J. Marco,* and *K. W. Ratts*, J. Am. Chem. Soc. *82*, 1260 (1960); *A. J. Speziale* and *K. W. Ratts, ibid. 84*, 854 (1962).
[2] *R. Rabinowitz* and *R. Marcus*, J. Am. Chem. Soc. *84*, 1312 (1962); *R. Appel, F. Knoll, W. Michel, W. Morbach, H. D. Wihler,* and *H. Veltmann*, Chem. Ber. *109*, 58 (1976); cf. *R. Appel*, Angew. Chem. *87*, 863 (1975); Angew. Chem. Int. Ed. Engl. *14*, 801 (1975).
[3] *R. Appel*, presented at the 25th IUPAC Congress, Jerusalem, July 10, 1975.
[4] *R. Appel* and *W. Morbach*, to be published.
[5] *F. Ramirez, N. B. Desai, B. Hansen,* and *McKelvie*, J. Am. Chem. Soc. *83*, 3539 (1961).

1-Naphthyl Rotation and Metal-Centered Rearrangement in Square-Pyramidal Molybdenum Complexes[1]

By *Henri Brunner* and *Joachim Wachter*[*]

In the thioamide complexes $C_5H_5(CO)_2MoSC(R)NR^*$ the Mo atom is a center of asymmetry[2]. Resolvable diastereoisomeric pairs are obtained with $R^* = (S)$-α-phenylethyl[2, 3]. At elevated temperatures the diastereomers undergo mutual interconversion *via* first-order intramolecular reactions[2, 4].

While the ^{1}H-NMR spectra of complexes with R = H, CH_3, and C_6H_5 show only two C_5H_5 singlets and two CH_3 doublets for each pair of diastereomers[5], twice as many signals are observed for the compound with R = 1-naphthyl. This is because each Mo configuration *(1)* and *(2)* forms two atropisomers *(1a)/(1b)* and *(2a)/(2b)* with the 1-naphthyl groups in different orientations[6].



The four isomers arise on reaction of $C_5H_5Mo(CO)_3Cl$ with (*S*)-(−)-*N*-(α-phenylethyl)-1-naphthothioamide in pyridine at 130 °C. The configurational isomers *(1)* and *(2)* can be obtained optically pure by fractional crystallization from ether/pentane (10:1)[5]. The sparingly soluble isomer *(1)* ($[\alpha]_{365}^{20} = -4035°$; 0.3 mg/ml in toluene) gives a ^{1}H-NMR spectrum (90 MHz, $CDCl_3$, −10 °C) containing two C_5H_5 signals at $\tau = 4.38$ and 4.46 (isomer ratio *(1a)*:*(1b)* = 81:19). The C_5H_5 signals of the readily soluble isomer *(2)* ($[\alpha]_{365}^{20} = +3135°$; 0.5 mg/ml in toluene) lie at $\tau = 5.05$ and 5.08 (isomer ratio *(2a)*:*(2b)* = 64:36). The splitting and intensities of the methyl signals resemble those for the C_5H_5 signals.

In $CDCl_3$ solution at 25 °C the intensity of the C_5H_5 signals of optically pure *(2)* gradually diminishes; a concomitant growth of the C_5H_5 signals of *(1)* progresses up to equilibration at *(1)*:*(2)* = 13:87. The time-dependence of the integrals (51 measurements)[7] affords the rate constants $k_{(1)\rightarrow(2)} = 5.36 \times 10^{-5} \pm 0.66 \times 10^{-6}$ s^{-1} and $k_{(2)\rightarrow(1)} = 9.19 \times 10^{-6} \pm 0.23 \times 10^{-6}$ s^{-1} as well as the activation energies $\Delta G^{\ddagger}_{(1)\rightarrow(2)} = 23.3 \pm 0.1$ kcal/mol and $\Delta G^{\ddagger}_{(2)\rightarrow(1)} = 24.3 \pm 0.1$ kcal/mol. The half-life of 184 ± 2 min for the equilibration *(1)* ⇄ *(2)* is comparable with the epimerization rates of other thioamide complexes[5]. Hence the observed process is ascribed to a configurational change at the Mo atom.

On heating of *(1)* or *(2)* in toluene solution the epimerization equilibrium is rapidly established ($\tau_{1/2}$ at 60 °C *ca.* 1.5 min, extrapolated). The C_5H_5 signals exhibit concomitant broadening. At 63 °C the dominant isomer *(2)* exhibits coalescence; at 80 °C the C_5H_5 signals of *(1)* and *(2)* are singlets, and the methyl signals doublets. The rate constants $k_{(2a)\rightarrow(2b)} = 2.31 \pm 1$ s^{-1} and $k_{(2b)\rightarrow(2a)} = 4.32 \pm 1$ s^{-1} and the activation energies $\Delta G^{\ddagger}_{(2a)\rightarrow(2b)} = 19.2 \pm 0.3$ kcal/mol and $\Delta G^{\ddagger}_{(2b)\rightarrow(2a)} = 18.8 \pm 0.3$ kcal/mol were calculated with the aid of the following parameters[8]: coalescence temperature $T_c = 336 \pm 0.3$ °K; linewidth $b_E = 0.6$ Hz; chemical shift $\Delta\nu = 2.63$ Hz (extrapolated to the coalescense temperature); equilibrium constant $K = 0.55 \pm 0.05$. This process is assigned to 1-naphthyl rotation in *(2)*. The much lower intensity of

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the C_5H_5 signals precludes accurate determination of the values for *(1)*.

In contrast to the 1-naphthyl complexes *(1)*/*(2)*, the corresponding 2-naphthyl complex does not appear to display any barrier to rotation. Each diastereomer gives only one C_5H_5 signal, which fails to split even on cooling to −80°C in [D_8]-toluene.

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CAS Registry numbers:
(1), 58919-14-5; *(2)*, 58957-77-0; $C_5H_5Mo(CO)_3Cl$, 12128-23-3

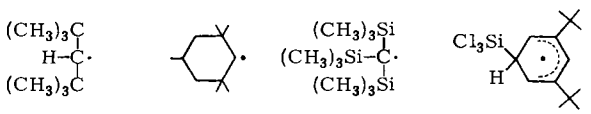
[1] Optically Active Transition Metal Complexes, Part 38. We are indebted to *T. Burgemeister* for recording the 90-MHz spectra. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. (*S*)-(−)-α-Phenylethylamine was kindly supplied by Dynamit Nobel, Troisdorf.—Part 37: *H. Brunner, W. A. Herrmann,* and *J. Wachter*, J. Organomet. Chem. *107*, C11 (1976).
[2] *H. Brunner*, Top. Curr. Chem. *56*, 67 (1975).
[3] *H. Brunner* and *W. A. Herrmann*, Chem. Ber. *105*, 3600 (1972).
[4] *H. Brunner* and *W. A. Herrmann*, Chem. Ber. *106*, 632 (1973).
[5] *H. Brunner* and *J. Wachter*, Chem. Ber., in press.
[6] Configurations in reaction scheme are arbitrary.
[7] KIN 2 Program (Fortran); *U. Kölle*, Dissertation, Universität Heidelberg 1969.
[8] *H. Kessler*, Angew. Chem. *82*, 237 (1970); Angew. Chem. Int. Ed. Engl. *9*, 219 (1970).

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

Persistent carbon-centered radicals are the theme of an article by *D. Griller* and *K. U. Ingold*. The authors suggest this term to symbolize radicals whose lifetime in solution is considerably longer than that of the methyl radical. Under certain experimental conditions the persistence of a radical can be expressed by the rate constant of its decomposition. Triphenylmethyl is a persistent radical; benzyl, vinyl, *tert*-butyl, *etc.*

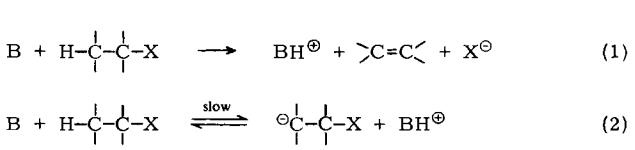


(1) *(2)* *(3)* *(4)*

are transient radicals. The thermodynamic stabilization or destabilization of a radical must be considered apart. After it had been shown that steric and non-electronic factors play the principal role in persistence, several persistent radicals were synthesized; examples are *(1)*—*(4)*. [Persistent Carbon-Centered Radicals. Acc. Chem. Res. *9*, 13—19 (1976); 46 references]

[Rd 845 IE—L]

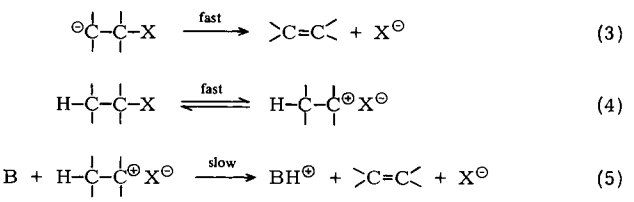
The distinction between concerted and nonconcerted eliminations is the subject of review by *E. H. Saunders, Jr.* A few years ago there was a certain amount of doubt that concerted reactions, especially E2 eliminations [Eq. (1)], are of frequent occurrence[*]. Instead, it was proposed that eliminations proceed according to the irreversible carbanion mechanism $(E1cB)_i$ [Eq. (2) and (3)] or the ion-pair mechanism $(E2)_{ip}$, [Eq. (4) and (5)]:



(1)

(2)

[*] *F. G. Bordwell*, Acc. Chem. Res. *3*, 281 (1970); *5*, 374 (1972).



(3)

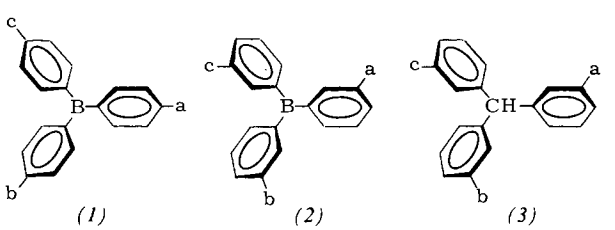
(4)

(5)

In an E2 process the β H atom is partly detached and the C—X bond partly opened in the transition state of the rate-determining step. It can be concluded from eliminations on β-deuteriated compounds and other experiments that almost all second order eliminations of simple primary and secondary derivatives follow the E2 mechanism. In tertiary and allylic derivatives or α-arylalkyl compounds it is still undecided whether or not the ion-pair mechanism is at issue in many cases. [Distinguishing between Concerted and Nonconcerted Eliminations. Acc. Chem. Res. *9*, 19—25 (1976); 68 references]

[Rd 846 IE—L]

The stereochemical consequences of correlated rotation in propeller molecules are dealt with in an article by *K. Mislow*. Examples are compounds of type *(1)*—*(3)* ($a \neq b \neq c$), whose substituents contain no stereoisomeric elements. Each rotation of a ring about the B-aryl or CH-aryl bond is accompanied by rotation of the other rings; this coupled motion is referred



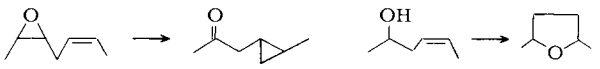
(1) *(2)* *(3)*

to as correlated rotation. Both the static and the dynamic stereochemistry of these molecules are first discussed. Three further sections of the article are devoted to stereochemical agreements, residual stereoisomerism, and residual stereotopism. [Stereochemical Consequences of Correlated Rotation in Molecular Propellers. Acc. Chem. Res. *9*, 26—33 (1976); 23 references]

[Rd 847 IE—L]

Some new chemical properties of unsaturated C_{18} acids are described by *F. D. Gunstone*. Particularly interesting are the

reactions involving neighboring group participation. Examples are the BF_3-induced transformation of epoxyalkenoic esters *(1)* into cyclopropane oxoesters *(2)* and the acid-catalyzed



(1) *(2)* *(3)* *(4)*

cyclization of polyhydroxy acids *(3)* to tetrahydrofuran derivatives *(4)*. (Only partial structures are given in each case.) [Some New Chemical Properties of Unsaturated C_{18} Acids. Acc. Chem. Res. *9*, 34—40 (1976); 26 references]

[Rd 848 IE—L]

A survey of hormone-receptor interactions has been written by *E. J. M. Helmreich*. It is not yet known how the hormone-receptor reaction is transformed into biological action. An important, though not universal, mechanism involves the activation of adenyl cyclase which generates the "second messenger" 3',5'-cyclic AMP. Hormone-receptor complexes are extremely long-lived; half-lives of 15 to 40 min have been measured for the complex of insulin. This tends to rule out any regulatory function of the complex in the overall process. It must therefore be asked how the interaction between hormone and receptor is modulated. One proposal is that of a negative cooperativity facilitating dissociation of the complex, and another one, applying in cases of positive cooperativity or none at all, assumes that regulation occurs beyond the stage of hormone-receptor interaction, say in an interaction between hormone-receptor complex and adenyl cyclase. [Hormone-Receptor Interactions. FEBS Lett. *61*, 1—5 (1976); 25 references]

[Rd 850 IE—R]

The bioenergetics of mitochondria in brown adipose tissue is considered by *D. G. Nichols*. In these cell organelles, found mainly in hibernating animals, a cold stimulus leads to generation of heat by oxidation of fatty acids. A mechanism must therefore exist for circumventing the coupling of oxidation rate to ATP production occurring in normal cells. This mechanism is seen in a nucleotide-dependent enhanced proton conductance by the membrane whose characteristics are in accord with *in vivo* thermogenesis. Uncertainty still surrounds the modulation of proton conduction *in vivo*. [The Bioenergetics of Brown Adipose Tissue Mitochondria. FEBS Lett. *61*, 103—110 (1976); 43 references]

[Rd 851 IE—R]

The legume storage proteins legumin and vicilin are the topic of an article by *E. Derbyshire, D. J. Wright*, and *D. Boulter*. Their localization and distribution in the seeds are described and methods for their extraction, purification, and characterization viewed in the light of modern biochemical practice. The physical, chemical, and immunological properties of the "classical" preparations from *Pisum sativum* are surveyed and compared with those of similar legumin and vicilin preparations from other leguminous plants. [Legumin and Vicilin, Storage Proteins of Legume Seeds. Phytochemistry *15*, 3—24 (1976); 271 references]

[Rd 853 IE—R]

BOOK REVIEWS

Molekülgeometrie. Elektronenpaar-Abstossung und molekulare Struktur (Molecular Geometry. Electron Pair Repulsion and Molecular Structure). By *R. J. Gillespie*. Translated by *J. Grobe*. Verlag Chemie, GmbH, Weinheim 1975. 1st Edit., xiii, 232 pp., 153 figs., 62 tables, paper, DM 29.80.

The Gillespie-Nyholm model concept of the consequences, to molecular geometry, of electron pair repulsion in the valence shell of molecules (*V*alence *S*hell *E*lectron *P*air *R*epulsion theory, VSEPR model) have proved extremely useful for systematizing the existing structural data and for predicting previously unknown structures. The simplicity of the model's principles promotes its use in teaching and study and makes the "theory" an important didactic and heuristic aid. It is therefore good to see this book by one of the model's founders, on the evolution and successes of the VSEPR concept, in a German translation. Thus, in an externally attractive form and at a reasonable price, teachers and students in the widest sense can discover for themselves the breadth of a concept whose beginnings go back to *G. N. Lewis*, but which has now been thought through afresh on the basis of much more extensive factual material. In so doing one is astonished to find how many structural details, often puzzling when looked at in isolation, can now be fitted in with very little difficulty.

This last phrase "with very little difficulty" must, however, be looked at more carefully for in spite of the very clear explanations and the many and successful illustrations, one cannot avoid the impression that things really cannot be quite so simple. The striking appeal of the model must not be allowed to overshadow the fact that much can indeed now be systematized anew, but fundamentally is not better "understood". This becomes clear on the introduction of ideas such as the "secondary valence shell" which is essential *e.g.* for the interpretation of the bonding state in the oxygen molecule. Here one would like to see some mention of the MO model which in its time was able to give a convincing answer to this problem. For such a courageous comparison of the capabilities of the relevant models one must wait until the last 15 pages, and then it is too late. It is hoped that the reader will not succumb to the temptation of this little book and willingly throw overboard all that he had previously learnt about bonding and structural matters: he may still need it.

Hubert Schmidbaur [NB 307 IE]

Biochemie (Biochemistry). By *A. L. Lehninger*. Translated by *K. Fischer* and *R. Ries*. Verlag Chemie, GmbH, Weinheim 1975. 1st Edit., xv, 747 pp., 468 figs., 94 tables, paperback DM 68.—, bound DM 78.—.

Since the first edition appeared four years ago, *Lehninger*'s "Biochemistry" has set a standard as the most comprehensive one-man textbook of biochemistry that is also modern in conception. This standard is confirmed by the almost universal agreement in reviews and has been exceeded by hardly any other textbook. Lehninger has rightly become the favorite textbook for the advanced biochemist, since it presents the coordinated filigree work of the functional interactions between cell components, *i.e.* the "molecular logic of the

organism", in an easy, readable, and nearly always correct manner. Verlag Chemie have taken the risk of bringing a translation of this compendium onto the much more limited German market, and have succeeded technically and linguistically, for one sees many students carrying the monster book and finds the fat blue volume in numerous libraries.

The advantage of the German translation is obvious, even for one who believes he gets on passably with English, for one can complete a search faster if one is not chasing linguistic details. The translation is consistently successful, even if a little lifeless; it misses the sparkling spirit and the rhythm of the original. On the other hand, the translators have also carefully but silently managed to remove many of the factual errors in the original and to extend the reference lists by numerous easily accessible reviews in the German literature and international monographs, thereby providing a real service to the German reader. The conversion of calories into joules is often carried out with excessive confidence in numbers, but the priggish and unspeakable "katal" is not yet included. The weaknesses of the original in the thermodynamic chapters, in the stereochemistry, and in the set problems naturally appear also in the translation, but these minor failings can be overlooked in view of the extraordinary didactic and factual merits of the book. Nevertheless, the avoidable externals are really disturbing: the oversize format of a pulpit bible—still harder to handle than the English edition—the poor contrast of the colors in many illustrations that are more vividly colored in the original, and above all the shiny yellow paper on which the whole book is printed; no one can work with it at night without troublesome and continuous adjustment, and anyone who likes to underline as an aid to memory will have no joy with this book. Finally, the purchaser will feel slightly cheated when he discovers that simultaneously with this translation an improved and expanded English edition has appeared at about half the price. All this hardly decreases the value of this textbook for the student, who will find in it much more than he is generally able to assimilate. In any case, the German Lehninger will undoubtedly become as greatly liked by students and teachers in Germany as its counterpart is in America, and that with complete justification.

L. Jaenicke [NB 308 IE]

Allgemeine und Anorganische Chemie (General and Inorganic Chemistry). By *V. Gutmann* and *E. Hengge*. Verlag Chemie, GmbH, Weinheim 1975. 2nd revised and expanded edit., xi, 397 pp., 160 figs., 124 tables, paperback DM 39.—.

In spite of all the enthusiasm with which "general chemistry" was introduced in recent years into various universities, this textbook also shows that general chemistry should not be taught in isolation from experimental chemistry. Accordingly, the material is divided into two parts: general chemistry and inorganic chemistry. The chapters in the first part describe: 1) atomic structure and the periodic system; 2) the nature of chemical reactions with new sections on free energy and reaction kinetics; 3) the chemical bond; this chapter has been extensively reworked from the first edition; 4) states of matter (such as gases, liquids, and solids) and crystal structure; 5) a newly arranged chapter on electron-acceptor-donor interactions which underlie the known concepts of redox reactions, coordination-chemical interactions, solubility, and ion formation. There follow: 6) acid-base considerations; 7) electrochemistry; 8) magnetochemistry, and 9) the structure of complexes (VB methods, ligand field theory, π-complexes).

The second part provides in terse form basic knowledge on the chemistry of the main-group and subgroup elements. To each section in the second part are added problems whose answers can be discovered from the text. Although some sections, *e.g.* those on the hydrogen spectrum, electronegativity, ion-exchangers, and magnetochemistry, are treated very briefly, this textbook contains much to stimulate the student and the teacher and can be recommended as a text to accompany a course on general and inorganic chemistry. Clear illustrations and carefully chosen tables aid understanding, particularly since the publishers have been able to improve the printing of the second edition.

Hk. Müller-Buschbaum [NB 310 IE]

Analysis of Water. By *J. Rodier*. Translated from the 5th French edition. Israel Program for Scientific Translations, John Wiley & Sons, New York—Toronto, and Keter Publishing House Ltd., Jerusalem 1975. 1st Edit., xvii, 926 pp., numerous figs. and tables, bound $ 76.50.

This analytical handbook is divided into the following main sections: analysis of natural waters (447 pp.), of waste waters (108 pp.), and sea water (by *Laporte* and *Kovacsik*, 42 pp.), bacteriological analysis (*Geoffray* and *Vial* 82 pp.), biological quality of fresh water (*Verneaux*, 23 pp.), and interpretation of results (78 pp.). In addition, there is an appendix (138 pp.), with sections on, *inter alia*, instrumental methods, statistical control and evaluation procedures, sediment analysis, degradation of detergents (not the OECD test), and numerous ancillary tables. The main chapters devoted to the three types of water are subdivided in the same way and consider sampling, immediate evaluation of a sample and determination of its physicochemical characteristics, and determination of the constituents and typical sum and action parameters by classical and modern methods (*e.g.* polarography, atomic absorption spectroscopy, use of ion-sensitive electrodes), including radioactive measurements. With respect to the bacteriological investigations, questions of collecting and handling the samples are treated, as well as testing for bacteria that indicate fecal pollution and important pathogens, while for the assessment of the water quality consideration is given to methods based on Saprobia systems, various fish tests, and biocenotic analysis.

The choice of the methods considered naturally shows individual streaks. Thus, the main weight is beyond doubt placed on the study of drinking water. The methods discussed there cannot, however, always be so simply applied to waste waters as is made to appear in Chapter 2. Furthermore, evaluation of the results of chemical analysis is restricted to one parameter and hardly at all concerned with comparable interpretation of several analytical values; this is unavoidable for usable and waste water in order to obtain information not directly measurable on the water under study. On looking through the book an error of translation—and a serious one—was noticed: "une eau résiduaire urbaine fraîche" for obtaining inoculation material for the BOD determination became "fresh urban tap water".

Considered as a whole, the book is a collection of prescriptions of wide range and notable completeness, in which, as the references cited show, the complete technical literature of the Western hemisphere has been considered, even if in particular German-language literature is not always given equal weight. Unfortunately, the work is not as up to date as would be desirable: the few citations from the 1970's are almost all from French sources, and very few of them are original papers. Thus, the book does not contain some important new developments, *e.g.* nitrification inhibition in the BOD determination; at the same time, it contains some data that have been revised, *e.g.* the table of temperature corrections for measurements of the electrical conductivity.

Rudolf Wagner [NB 313 IE]

ANGEWANDTE CHEMIE
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Volume 15 · Number 6
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Pages 321–390

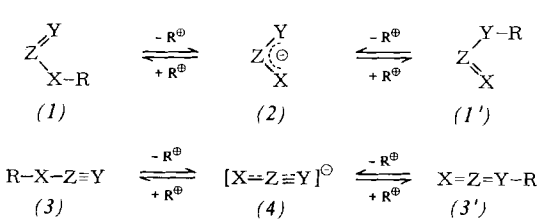
The Concept of Allopolarization. Effects of Substituents on the Reactions of Ambifunctional Anions

By Rudolf Gompper and Hans-Ulrich Wagner[*]

The chemistry of ambifunctional anions is of great importance in organic preparations. Planning of syntheses requires a set of rules correlating structure and selectivity. The concept of allopolarization permits a description of substituent effects on kinetically controlled reactions: the change in selectivity is a function of the change in polarity of the ambifunctional anions. The relative charge density $P = l_X/l_Y$ serves as "polarity index"; X and Y are the potential sites of reaction. An attempt is made to illustrate the utility of this principle by means of examples taken from various classes of compounds.

1. Introduction

Owing to their great preparative significance in all areas of chemistry, the reactions of ambifunctional (ambident[11]) compounds have always posed a mechanistic challenge to the chemist (cf. refs. [1–14]). The term "ambifunctional" cannot easily be defined unequivocally; the following statements are restricted to conjugated systems of the general formulas *(1)*, *(1')* and *(3)*, *(3')*, and in particular to the



anions *(2)* and *(4)*. Compounds *(1)* to *(4)* characteristically react with electrophiles in positions 1 *or* 3, *i.e.* at X *or* Y.

A concept common to all theories of ambifunctional reactivity is that two factors are primarily responsible for product formation, *viz.* the polarity (charge, "hardness") of the two reactants on the one hand, and their polarizability (frontier orbital coefficients, "softness") on the other. This dualism has been expressed particularly clearly in the concept of hard and soft acids and bases (HSAB concept)[13] and in the idea[9, 10, 12, 14] that the chemical reactivity results from the interplay of "charge control" and "orbital control".

Apparently limited in scope, the HSAB concept, which reflects the formal distinction between covalent and heterovalent bonds, has its champions[15] and its critics[16]. The problems encountered in applying it to the reactions of ambifunctional compounds are clear from Scheme 1 (substituent effects being neglected).

a) The HSAB concept makes no distinction between kinetic and thermodynamic control, although different products are formed in many cases.

b) The "hardness" of the site X has a differential effect upon the reactions of the uncharged compounds and their anions (amides, for instance, are *O*-alkylated on kinetic control, while amide anions are *N*-alkylated).

Similar difficulties are seen on examining the "perturbational treatment of chemical reactivity"[9, 10, 12, 14] for its applicability to the planning of syntheses. Any decision whether charge or orbital control predominates in a reaction is usually reached

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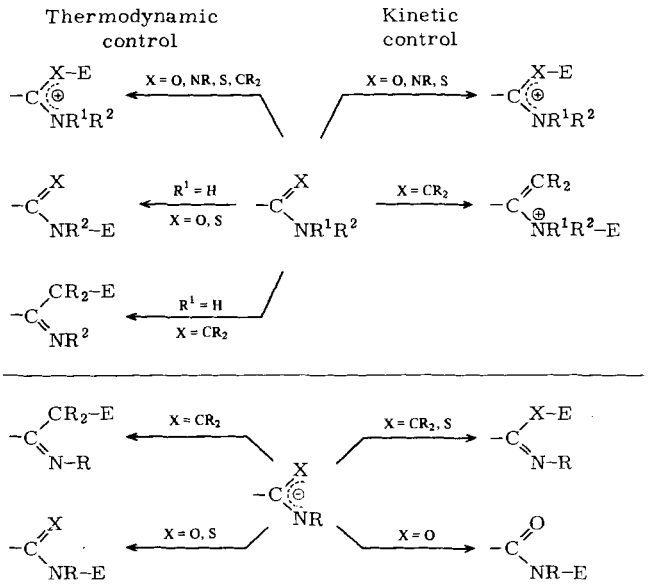
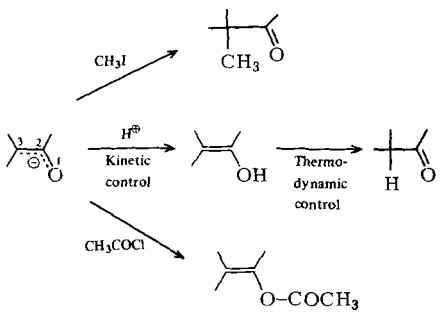


Scheme 1. Reactions of some ambifunctional systems with electrophiles ($E^{\oplus}$).

a posteriori on the basis of experimental results. At best, crude predictions of reactivity are possible for entire classes of compounds, for instance, the enolate ions shown in Scheme 2.



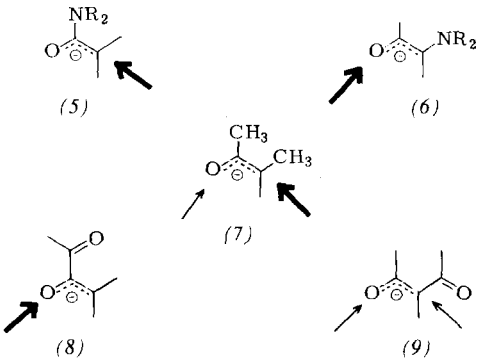
Scheme 2. Reactions of the enolate ion. Frontier orbital coefficients: $c^2_{3,\mathrm{HOMO}}=0.543$, $c^2_{1,\mathrm{HOMO}}=0.349$; charge densities $l_3=-0.301$, $l_1=-0.785$.

Formation of enols on kinetically controlled protonation (ketones usually have the greater thermodynamic stability) and occurrence of enol esters on acylation with acyl chlorides and carboxylic anhydrides[17] can be interpreted by the hardness of HX and RCO—X as electrophiles; they consequently undergo charge-controlled reaction with the enolate O atom which bears the major part of the negative charge.

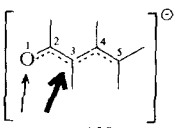
In comparison with HX and RCO—X, methyl iodide is a "soft" nonpolar reagent. Since C-3 of the enolate ion has the greatest frontier orbital coefficient we would expect *C*-methylation in this case.

Owing to the electronegativity difference between O and C, the gradation of reactivity indices (charge l and frontier orbital coefficient c^2_{HOMO}) corresponds in all enolate ions without exception to the values given in the legend of Scheme 2. However, variation of the substituent as in the enolate ions *(5)*—*(9)* (Scheme 3) drastically alters their mode of reaction under comparable conditions (the arrows symbolize the relative yields and the site of alkylation). The frequently assumed correlation[18] between increase of *C*-alkylation and decrease in acidity of the keto compound is not evident.

Another result[17] difficult to reconcile with the "charge-orbital concept" is that dienolate ions *(10)* of electrophiles are attacked mainly at C-3, occasionally at the O atom, but never at C-5 under kinetic conditions, regardless of the nature of the electrophile.



Scheme 3. Reactions of substituted enolate ions.



(10)

Position	l	c^2_{HOMO}
1	−0.730	0.208
3	−0.230	0.301
5	−0.186	0.356

Attractive as the HSAB concept, and the related perturbational charge-orbital concept, may appear for the interpretation of chemical bonding in the ground- and transition state, its application to the reactions of ambifunctional compounds, and particularly to the treatment of the substituent effects in anions, is beset with difficulties. It is precisely in the interpretation of substituent effects on the course of chemical reactions, however, that theoretical concepts reveal their heuristic value to the preparative chemist.

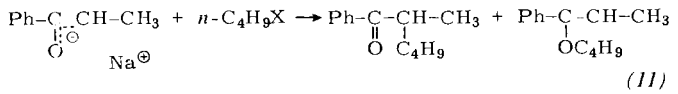
2. Derivation of the Concept of Allopolarization

The difficulties attending application of two-parameter models to the chemistry of ambifunctional systems sharply contrast with the resounding success of orbital symmetry rules for concerted reactions (*Woodward-Hoffmann*[19], *Fukui*[20], *Klopman*[21], *Dewar*[22], *Zimmerman*[23]). Subsequent refinements or additions (cf., *e.g.* ref. [24]) have not detracted from the significance of the original concept which utilizes a single parameter. Astonishing as it may seem, substituent effects can even be neglected in many cases.

Assuming that orbital interactions occur preferentially over short distances between reacting centers while Coulombic interactions predominate at greater distances, it might be expected that the majority of bimolecular reactions of polar systems—and such are the reactions of ambifunctional compounds—will be charge-controlled. This should be all the more true for reactions of charged species.

Might there not therefore be some set of rules governing the reactions of ambifunctional anions (and cations), comparable in simplicity to the Woodward-Hoffmann rules, which are based on the control of product formation by charge interaction instead of on the principle of orbital-symmetry control in concerted reactions? Such rules would not be required to give any detailed "explanation" for the formation of chemical bonds. The possibility of predicting with their aid how the product composition of a kinetically controlled reaction would alter on changing the substituents in the reactants and solvent would be entirely sufficient.

The basis for a set of rules permitting the description of the chemical behavior of ambifunctional anions can be taken from Table 1: The course of butylation of propiophenone anion depends upon the solvent and upon the alkylating agent[34].



(11)

Table 1. *C*- and *O*-alkylation of the propiophenone anion with *n*-butyl derivatives in various solvents. (HMPT = hexamethylphosphoric triamide, DMSO = dimethyl sulfoxide, THF = tetrahydrofuran.) Yields Q_O [%] of enol ether *(11)* are given.

X	HMPT	DMSO	THF	Diglyme	Et_2O
I	15	10	3	4	1
Br	40	23	5	5	5
Cl	67	46	31	13	18
OSO_3CH_3	83	—	—	—	11
OTos	85	44	—	—	20
OPO_3Bu_2	93	78	40	—	36

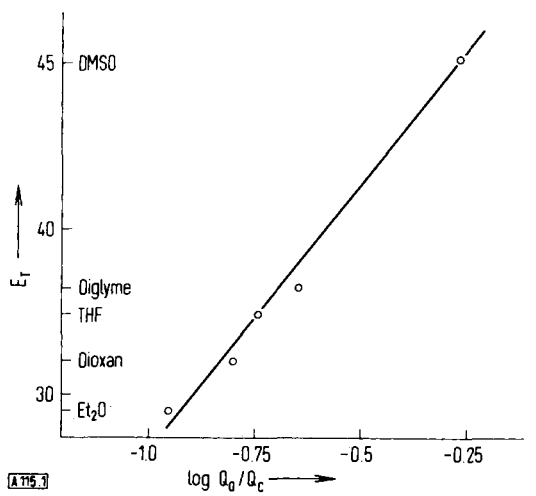


Fig. 1. Relationships between the yield Q_O of enol ether *(11)*, the yield Q_C of *C*-butylated propiophenone, and the solvent parameter E_T (see Table 1). $\log Q_O/Q_C = 0.06532 \times E_T - 3.1783$. $\log Q_O/Q_C$ is also designated the selectivity factor S_f.

The yield of enol ether *(11)* correlates well with the solvent parameter E_T (see Fig. 1). Increasing solvent polarity increases the yield of *(11)*. Hence it may be deduced that increasing solvent polarity enhances charge control which in turn favors electrophilic attack at the O atom of the enolate ion. Similar observations have been made with other enolate alkylations[17,25-30]. The solvent affects the rates of *O*- and *C*-alkylation not only *via* the change in solvation of starting materials and transition states but also *via* the change in bonding in the metal enolates (covalent bond/contact ion pairs/solvent separated ion pairs/free ions)[30-32]. *LeNoble*[29] summarized his findings for salts of acetoacetic esters in a single sentence: "The freer the anion, the larger the O/C ratio".

A similarly drastic change in the yield of enol ether is observed on use of different alkylating agents. In all solvents the yield of enol ether increases in the order R—I < R—Br < RCl < R—OY ≤ (R—F): the yields differ relatively slightly for the compounds R—OY; the main requirement appears to be that an O function is bound to the group R.

In keeping with the interpretation of the solvent effect, the effect of the alkylating agent could be explained in terms of an increasing polarization of the C—X bond in R—X raising the partial positive charge at the α-C atom, as a result of the increasing electronegativity, and thus enhancing the effect of charge control.

Other research groups have also reported high yields of enol ethers on reaction of enolates with dialkyl sulfates and triethyloxonium tetrafluoroborate[17,26,28,33]. However, the assumption[28] that the *O*/*C*-alkylation ratio increases with increasing reactivity of the alkylation finds no confirmation. The reactivity decreases rapidly along the series Bu—I > Bu—Br > Bu—Cl > Bu—F, but the yield of enol ether increases (see Table 1). Reaction of the propiophenone anion with the highly inert compound *n*-butyl fluoride in HMPT affords *ca.* 96% of the enol ether[34], *i.e.* more than with the very reactive triethyloxonium tetrafluoroborate. The relation between reactivity of the alkylating agent and the selectivity of their reaction with enolate ions is apparent from Table 2. Thus the energy of the transition and the heat of reaction[36] appear to be of minor importance for the selectivity of reactions of ambifunctional anions. The change in the *C*/*O*-alkylation ratio has also been explained as arising from the change in "hardness" of the electrophile due to the leaving group[35,37].

Table 2. Reaction of Na-acetoacetic ester with C_2H_5—X in dimethoxyethane [35].

X	I	Br	TosO	$EtOSO_3$	CF_3SO_3	FSO_3
$k \times 10^5$ [l mol^{-1} min^{-1}]	500	8	1.3	40	6.1×10^5	17.8×10^5
Q_C/Q_O	>100	60	6.6	4.8	3.5	3.7

The essence of all the previous arguments is that increasing the polarity of the solvent on the one hand, and of the electrophile on the other, enhances charge control on alkylation of enolate ions and hence favors attack by the alkylating agent on the O atom as the site of greater negative charge. Development of this idea implies that an increase in polarity of the enolate ion should also lead to an enhancement of charge control. It then remains to be defined what the "polarity" of an ambifunctional anion actually signifies. We propose the use of the relative charge density *P* or the relative charge difference *P'* as a polarity index (the HMO charges are employed in the following discussions, generally being the easiest to calculate[37a]):

$$P = l_X/l_Y$$
$$P' = (l_X - l_Y)/(l_X + l_Y)$$

X and Y are the potential reactive sites [see *(2)* and *(4)*].

The utility of this proposal is confirmed by Figure 2[38]: the extent of *O*-methylation increases with increasing polarity index $P = l_O/l_C$ of the *para*-substituted propiophenone anions.

Donor- and acceptor substituents appear to modify the polarity (polarity index *P*) of ambifunctional anions and thus affect the product ratio of reactions with electrophiles (kinetic control).

The reaction of the ambifunctional anion *(2)* with the electrophile E is illustrated in Scheme 4. The ratio of the yields of the two products *(12)* and *(13)* affords the selectivity factor S_f. Replacement of the anion *(2)* by the substituted anion *(2')* modifies the polarity index $[P_{(2)} - P_{(2')}]$. The crux of the allopolarization concept is that the *change*

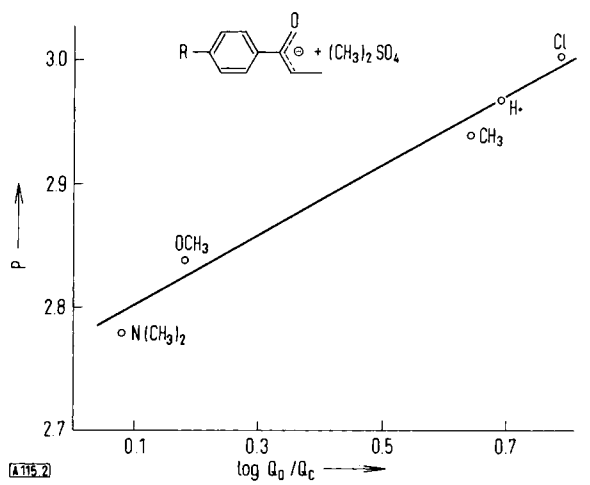
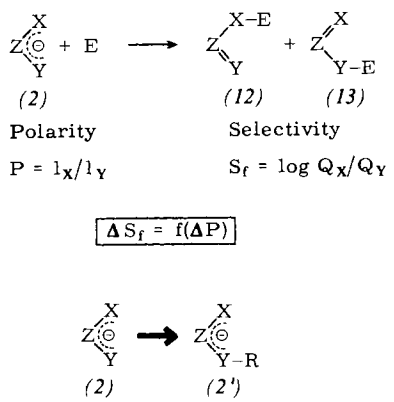


Fig. 2. Relationships between the yield Q_O of enol ether, the yield Q_C of *C*-methylated *p*-propiophenone and the polarity index $P = l_O/l_C$ of *p*-substituted propiophenone anions. $\log Q_O/Q_C$ is also designated the selectivity factor S_f.



Scheme 4. Concept of allopolarization of ambifunctional anions.

in selectivity is a function of the change in polarity. If P increases on substitution $[P_{(2)} < P_{(2')}]$ then the charge control is enhanced and attack by the electrophile at the center of greater negative charge (X or Y) is favored. If P becomes smaller $[P_{(2)} > P_{(2')}]$ then charge control is diminished and electrophilic attack is favored at the site bearing the smaller charge.

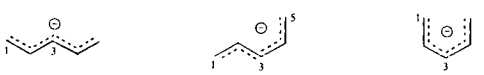
Table 3 gives an impression of the way in which donor and acceptor substituents affect the distribution of charge in ambifunctional anions (cf. ref. [39]). It should be noted that a) the influence of strong acceptors on the amidine anion system (X,Y = NR) differs from that on the allyl anion system and b) donor and acceptor groups can modify the polarity index in the same way.

3. Application of the Allopolarization Concept

The allopolarization principle will now be illustrated with the aid of examples. The sheer mass of experimental data precludes our consideration of finer details.

3.1. Allyl Anions

The reactions of allyl anions can be excellently described in terms of charge distribution: the charge densities in the pentadienyl anions *(14)*—*(16)* accord with the course of



Pople-π-SCF:			
l_1	−0.40	−0.42	−0.34
l_3	−0.36	−0.38	−0.39
l_5		−0.39	

protonation and reactions with methyl iodide and ethylene oxide[17,40–47]. Hydrolysis of the anions *(17)*[48] and *(18)*[49] also complies with the charge distribution (Table 4).

Considerable preparative significance attaches to the reactions of 1-substituted allyl anions with electrophiles. As shown in simplified manner in Scheme 5, the site of electrophilic attack corresponds to the points of greatest charge density according to Table 3: donor substituents direct electrophiles into position 3, and acceptor substituents into position 1. Deviations from this scheme are usually attributable to steric

Table 3. Charge distribution (positions 1 and 3) in ambifunctional anions (HMO, $\alpha_R = \alpha + 1.0\ [\beta]$). To save space all zeros preceding the decimal points have been omitted.

α_R [β]	R		R–X		R–X		R–X		R–X–X		R–X–X		R–X–X	
a) R = Acceptor														
	−.500	−.500	−.785	−.301	−.333	−.333	−.301	−.785	−.785	+.086	−.667	−.667	+.086	−.785	−.500	−.500
−8.	−.534	−.464	−.784	−.284	−.405	−.256	−.345	−.766	−.789	+.116	−.675	−.655	+.019	−.751	−.532	−.468
−4.	−.532	−.424	−.758	−.265	−.437	−.176	−.360	−.746	−.766	+.144	−.661	−.644	−.027	−.715	−.536	−.440
−2.	−.473	−.344	−.695	−.231	−.418	−.036	−.342	−.708	−.700	+.188	−.618	−.625	−.072	−.643	−.518	−.397
−1.	−.333	−.229	−.600	−.181	−.297	+.132	−.271	−.653	−.598	+.241	−.552	−.600	−.083	−.536	−.437	−.344
0.	−.000	−.000	−.374	−.040	+.040	+.374	−.034	−.529	−.354	+.354	−.387	−.537	+.036	−.277	−.333	−.229
b) R = Donor														
	−.500	−.500	−.785	−.301	−.333	−.333	−.301	−.785	−.785	+.086	−.667	−.677	+.086	−.785	−.500	−.500
+8.	−.453	−.530	−.766	−.318	−.252	−.403	−.250	−.801	−.758	+.055	−.639	−.678	+.148	−.813	−.447	−.534
+4.	−.419	−.555	−.751	−.332	−.191	−.461	−.215	−.814	−.733	−.023	−.617	−.688	+.182	−.836	−.401	−.569
+2.	−.375	−.591	−.729	−.357	−.118	−.547	−.176	−.832	−.691	−.038	−.585	−.706	+.200	−.867	−.333	−.633
+1.	−.333	−.633	−.703	−.389	−.063	−.642	−.146	−.854	−.633	−.138	−.550	−.732	+.179	−.897	−.276	−.724
0.	−.276	−.724	−.642	−.490	−.063	−.805	−.138	−.896	−.500	−.500	−.490	−.805	+.034	−.944	−.333	−.896

Table 3. (Continued).

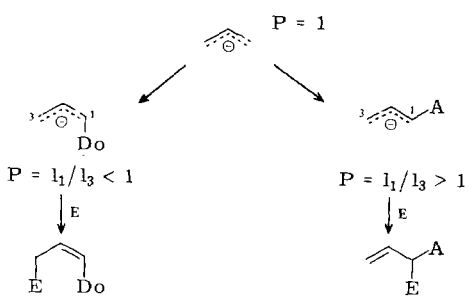
α_R [β]	R	R, X	R, X	R, X	R, X, X	R, X, X	R, X, X	R, X, X
a) R = Acceptor								
		−.785 −.301			−.785 +.086			
−8.		−.783 −.255			−.790 +.132			
−4.		−.786 −.210			−.798 +.173			
−2.		−.796 −.126			−.813 +.238			
−1.		−.816 −.000			−.832 +.322			
0.		−.847 −.400			−.841 +.546			
b) R = Donor								
		−.785 −.301			−.785 +.086			
+8.		−.789 −.344			−.783 +.037			
+4.		−.795 −.379			−.784 −.010			
+2.		−.805 −.431			−.789 −.092			
+1.		−.818 −.488			−.800 −.200			
0.		−.847 −.600			−.841 −.454			

(17) (18)

Table 4. Charge distribution in the anions (17) and (18) and relative yields of hydrolysis product [48, 49].

	(17)			(18)	
	Charge	Yield [%]		Charge	Yield [%]
C-1	−0.163	—	C-1		—
C-2	−0.180	64	C-2	−0.197	24.5
C-3	−0.175	26	C-3	−0.056	—
C-6		—	C-4	−0.201	74.5
C-7	−0.101	10	C-5	−0.063	—
			C-9		

hindrance. Apart from that, ion pair effects (see, *e.g.*, refs.[50–52]) may also be operative as a result of "blocking" of the more highly charged C atom by the metal ion (cyclic concerted alkylations with RX, however, are unfavorable[53]).

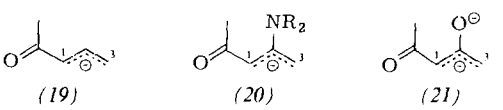


Scheme 5. Reactions of 1-substituted allyl anions with electrophiles. Do = donor = $CR_2^{\ominus}$ [54], $O^{\ominus}$ [55], $S^{\ominus}$ [56], NR_2 [57–62], OR [63–65], CH_3 [57, 66]; A = acceptor = BR_2 [67], SiR_3 [68, 69], SR [70–72], SOR [71, 72], SO_2R [73], $PO(OR)_2$ [74], COR [17, 75], CO_2R [76], CN [17], C_6H_5 [77, 78].

The reactions of allyl anions with carbonyl compounds often take a different course from those with alkylating and acylating agents. Alkyl-substituted allyl anions, for example, are preferentially attacked at the alkyl-substituted C atom in the absence of steric hindrance[50]. 1,1-Dichloroallyllithium reacts with aldehydes and ketones in the α- and/or γ-position[79]. The exceptional situation in the case of carbonyl compounds probably arises from their tendency to undergo multicenter processes on the one hand and thermodynamically controlled reactions on the other.

γ-Alkylation of 1-acylallyl anions can be accomplished under kinetic conditions in two different ways:

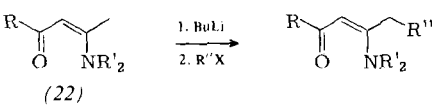
1-Acylallyl anions are employed which bear a donor substituent in position 2. In the allylic component of the anions (19) the greater negative charge is located at C-1, but at



(19) (20) (21)

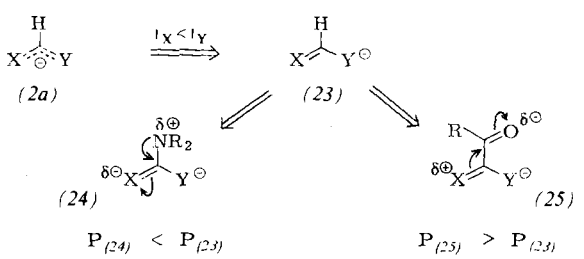
	(19)	(20)	(21)
l_1	−0.230	−0.245	−0.249
l_3	−0.186	−0.298	−0.381
P	1.236	0.822	0.654

C-3 in the allylic part of the anions (20) and (21). According to the concept of allopolarization, dianions of β-dicarbonyl compounds corresponding to type (21) undergo γ-alkylation[80, 81]. Reaction of enamino ketones (22) *via* (20) follows the same pattern[82–85].



(22)

The influence of 2-substituents on the polarity of (2a) can be deduced without explicit calculation (see Scheme 6).



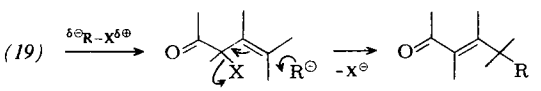
Scheme 6. Effect of 2-substituents on polarity (polarity index P) of anions (see text for details).

The starting point is that resonance structure of *(2a)* which best represents the charge distribution; *i.e.* *(23)* in the case of $l_X < l_Y$. Introduction of a donor substituent (NR_2) into position 2 of *(23)* yields the formula *(24)* in which X is assigned a negative partial charge. Thus $P_{(24)} < P_{(23)}$; weaker charge control and an enhanced proclivity to undergo reaction at X are the consequences. The reverse applies on going from *(23)* to *(25)*: charge is withdrawn from X by the acceptor substituent (COR), *i.e.* $P_{(25)} > P_{(23)}$. The increase in charge control then results in a comparatively greater tendency to react at Y.

It should be noted in this context that the reactions of anions of type *(19)* can also be described with the aid of formula *(26)* (similar alternatives are also available for other systems). *(26)* is a vinyl-substituted enolate ion. Since the

vinyl group is only a weak acceptor, *(26)* will be expected to display reactions similar to those of the unsubstituted enolate ion, *i.e.* mainly *C*-alkylation (see Section 3.4). The preparative problem at hand will determine which of the formulas is to be preferred; the predictions are essentially the same.

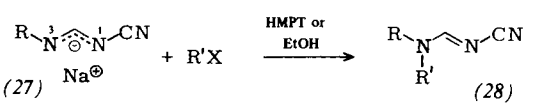
The use of allofunctionalized alkylating agents ("umpolung") also permits γ-alkylation of anions of type *(19)*[86].



2-Azaallyl anions react similarly to allyl anions. Mention should be made of the reactions of anions of 5-oxazolones[87] and the alkylation of metalated *N*-[bis(alkylthio)methylene]-α-amino carboxylic esters[88].

3.2. Amidine Anions

With respect to the active sites, amidine anions have the same symmetry as allyl anions. However, strong acceptor substituents have a different polarizing effect in the two systems (Table 3). Since N-3 bears the greater negative charge in 1-acceptor substituted amidine anions, electrophiles should attack preferentially at that site. This is indeed the case, as demonstrated by the reactions of the Na salts *(27)* of cyano-

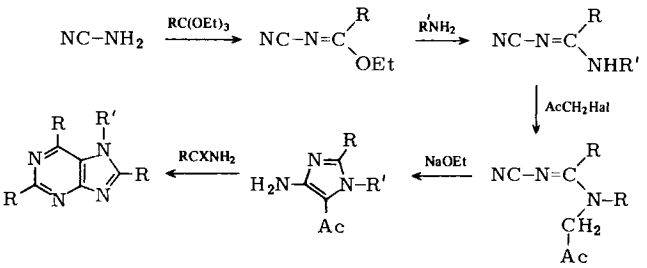


R = $C_6H_5CH_2$, *i*-C_3H_7, *t*-C_4H_9, C_6H_5, *p*-$CH_3C_6H_4$, *p*-$CH_3OC_6H_4$, *p*-$EtO_2CC_6H_4$, β-$C_{10}H_7$, 2-pyridyl

R'X = CH_3I, $(CH_3)_2SO_4$, $PhCH_2Cl$, $PhCOCH_2Br$, $NCCH_2Br$, EtO_2CCH_2Br

formamidines—only the cyanamidines *(28)*[38,39] are produced. Selective formation of *(28)* can be exploited for a facile synthesis of 4-amino-5-acylimidazoles and purines[89] (see Scheme 7).

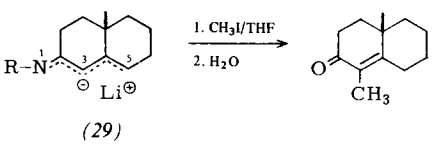
Methylations of the Na salts of phosphorus compounds $(EtO)_2PNHAryl(=NAryl)$[90] follow the same pattern as the reactions of *(27)*.



Scheme 7. Synthesis of imidazoles and purines *via* amidines. R = H, alkyl, aryl, SR, NR_2. Conversion of 4-amino-5-acylimidazole into purine can also be accomplished with RNCX or H_2N—CX—NH_2; X = O or S.

3.3. Enamine and Hydrazone Anions

Like enolate ions, simple enamine anions undergo preferential *C*-alkylation[91-94]; the extent of *N*-alkylation can be greatly increased by use of especially polar alkylating agents such as triethyloxonium fluoroborate[93]. Alkylations of anions of 5,6-dihydro-2,4,4,6-tetramethyl-4*H*-1,3-oxazine[95,96] and of 2-methyloxazolines[97] possess particular preparative importance. Dienamine anions[98] such as *(29)* are only α-alkylated in the same way as dienolate ions *(10)*.

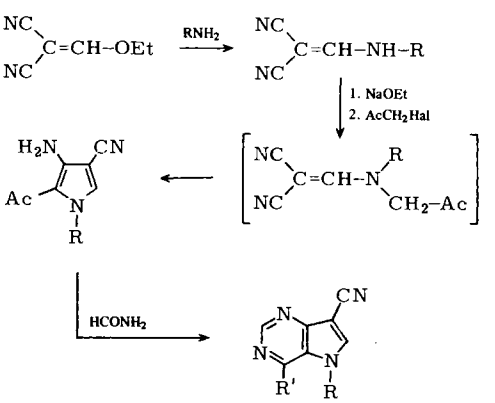


(29)

The presence of donor and acceptor substituents at C-3 raise the polarity of the enamine anions (see Table 3). Alkylation of the dianion *(30)* can be regarded as an example of the donor case[99].

(30)

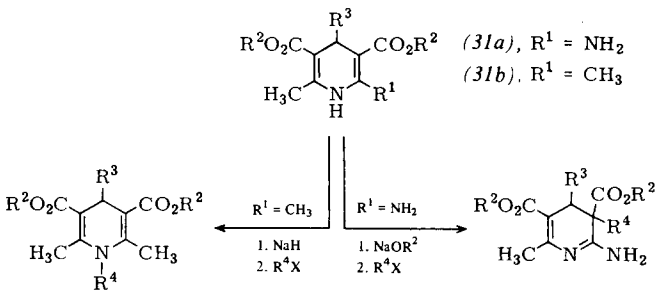
3-Acceptor substituted enamine anions are obtained, *e.g.* from aminomethylenemalononitriles. Their exclusive *N*-alkylation can be utilized for synthesizing aminopyrroles and pyrrolo[3,2-*d*]pyrimidines[89], as shown in Scheme 8.



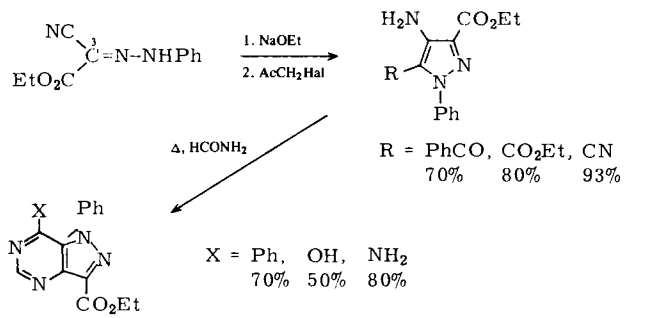
Scheme 8. Synthesis of aminopyrroles and pyrrolo[3,2-*d*]pyrimidines *via* enamines. R' = C_6H_5, 2-thienyl, CH_3, OH.

The effect of a change of substituent at position 2 of the enamine anion to be expected from the general scheme is

confirmed by the reactions of the anions of *(31a)*[100] and *(31b)*[101–103].

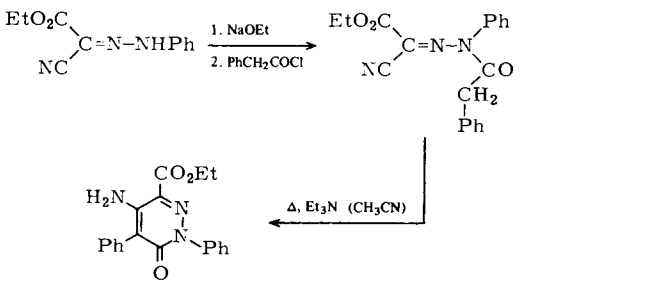


The principle of the aminopyrrole synthesis shown in Scheme 8 can also be employed for production of aminopyrazoles and pyrazolo[4,3-*d*]pyrimidines from hydrazone anions according to Scheme 9[104] (1-alkylation; further reactions of hydrazone anions, see Section 3.6).



Scheme 9. Synthesis of aminopyrazoles and pyrazolo[4,3-*d*]pyrimidines from hydrazones.

Acylation of hydrazone anions (see Scheme 10) corresponds to their alkylation; pyridazine derivatives can be synthesized in this way[104].



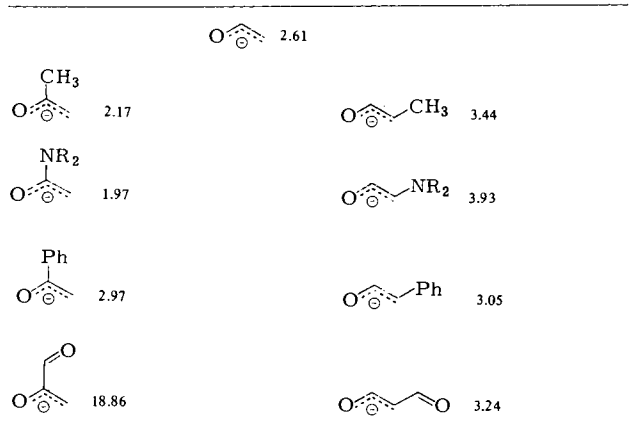
Scheme 10. Synthesis of pyridazines from hydrazones.

3.4. Enolate Ions

Apart from the reactions of allyl anions, those of enolate ions[17] (see also Sections 1 and 2) provide considerable material for discussions of the substituent effect. Table 5 conveys an impression of the polarity indices of typical enolate systems. Unfortunately, only little is known about aldehyde anions[91c, 105]. Since the Na salt of phenylacetaldehyde is only *O*-methylated in DMSO[28], *O*-alkylation should generally predominate with aldehyde anions in dipolar aprotic solvents according to the polarity indices.

Expectedly, the reaction of all enolate ions with trimethylchlorosilane only affords enol derivatives[106–111].

Table 5. Polarity indices $P = I_O/I_C$ of some enolate systems.



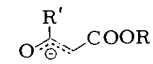


Table 6. Influence of substituents in position 2 of 3-alkoxycarbonyl enolate ions on the reaction with ethyl iodide and with ethyl *p*-toluenesulfonate (both in HMPT). Yields of OEt derivative are given. $P = I_O/I_C$. R = alkyl.

R′	I_O	I_C	P	with EtI	with EtOTos
				Yield [%]	
CO_2R	−0.655	−0.112	5.85	—	100 [38] [a]
CF_3				—	100 [26]
H	−0.647	−0.200	3.25	—	100 [38] [a]
CH_3	−0.687	−0.261	2.63	13	88 [26]
OR				— [38] [a]	
NR_2	−0.698	−0.235	2.97		—

[a] With dimethyl sulfate.

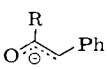
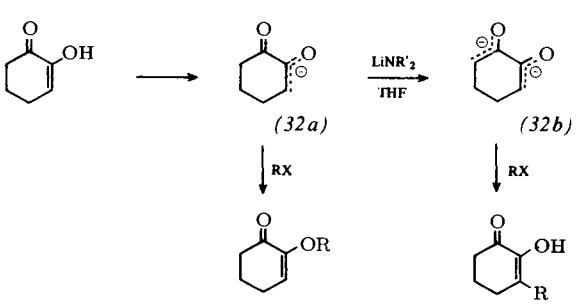


Table 7. Influence of substituents in position 2 of 3-phenyl enolate ions on the reaction with dimethyl sulfate in HMPT. $P = I_O/I_C$; Q_O = yield of OCH_3 derivative, Q_C = yield of CCH_3 derivative.

R	P	Q_O/Q_C
C_6H_5	3.55	> 10
H	3.05	> 10
CH_3	2.55	0.7
OCH_3	2.49	< 0.1
$O^{\ominus}$	2.22	< 0.1

The influence of substituents in position 2 of enolate ions follows from Tables 6 and 7. The relationship between polarity and selectivity is also impressively demonstrated by the fact that the monoanions [*e.g. (32a)*] of 1,2-cycloalkanediones are *O*-alkylated[112, 113], while the dianions [*e.g. (32b)*] are *C*-alkylated[114].



The situation is not so clear-cut for substituents in position 3, probably due mainly to steric factors. Table 8 surveys methylations of anions of substituted acetophenones. The difference in yield between R = *i*-C_3H_7 and $N(CH_3)_2$, which have the same steric bulk, reflects the more pronounced donor effect of the amino group. Exclusive *O*-methylation in the case of the two *N*-substituted compounds can be explained by an increase in polarity of the enolate ion caused by donor and acceptor substituents. However, a considerable difference in reactivity exists between R = $\overset{\oplus}{N}(CH_3)_3$ and $\overset{\oplus}{P}Ph_3$ on the one hand and R = $\overset{\oplus}{S}(CH_3)_2$ on the other (it should be borne in mind that among these three substituents only that containing sulfur still possesses a lone pair)[115].

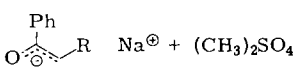


Table 8. Influence of substituents in position 3 of acetophenone anions on the reaction with dimethyl sulfate in HMPT at 25°C. Substituents of comparable bulk are shown linked together.

R	Yield [%] OCH_3 derivative	Yield [%] CCH_3 derivative
H [a]	82	18
COPh	70	30
n-C_3H_7	85	15
i-C_3H_7	85	15
t-C_4H_9	100	
$N(CH_3)_2$	100	
$\overset{\oplus}{N}(CH_3)_3$	100	
SPh	100	
$\overset{\oplus}{S}(CH_3)_2$		100
SOPh	100	
SO_2Ph	40	60
$\overset{\oplus}{P}Ph_3$ [b]	100	

[a] K salt.
[b] With C_2H_5I [116].

In other systems *C*-alkylations of the anions of α-mercapto ketones are also possible[118–120]; dimethylsulfonium benzoylmethanide is *O*-methylated by trimethyloxonium tetrafluoroborate[121].

A certain degree of uncertainty surrounding some reactions of *S*- and *P*-substituted enolate ions prompts us to ask the question whether it might not be more appropriate to use an "orbital index" $F = c^2_{C,\,HOMO}/c^2_{O,\,HOMO}$ (cf. ref. [122]) instead of the polarity index $P = l_O/l_C$. The changes in the two indices are compared in Figure 3. The *P* value is seen to be highly sensitive to a change of substituent, whereas the *F* value appears relatively insensitive. The same applies to allyl anions (see Fig. 4). Hence the *P* value appears to be better suited than the *F* value for demonstrating relations between structure and reactivity/selectivity.

The influence of aromaticity can also be regarded as a "substituent effect". Table 9 lists some anions in which the enolate moiety is incorporated into (anti)aromatic/bicycloaromatic systems. Aromatic systems predictably have large polarity indices, and antiaromatic systems small ones (phenolate ions are generally *O*-alkylated and *O*-acylated). The fact that the anions of anthrone[123a] and of phloroglucinol[123b] can be *O*- and/or *C*-alkylated is reflected in the decrease in polarity indices upon annelation of a benzene ring on the α-naphtholate ion or upon introduction of a *m*-hydroxy group into the resorcinol monoanion.

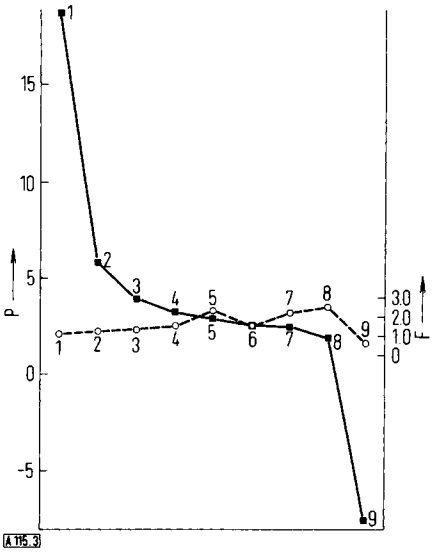
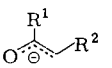


Fig. 3. Comparison of the polarity index $P = l_O/l_C$ (——) and the "orbital index" $F = c^2_{C,\,HOMO}/c^2_{O,\,HOMO}$ (– – –). The indices compared are those for substituted enolate ions of the type



1: $R^1 = CO_2R$, $R^2 = H$; 2: $R^1 = R^2 = CO_2R$; 3: $R^1 = H$, $R^2 = NR_2$; 4: $R^1 = H$, $R^2 = CO_2R$; 5: $R^1 = NR_2$, $R^2 = CO_2R$; 6: $R^1 = R^2 = H$; 7: $R^1 = R^2 = NR_2$; 8: $R^1 = NR_2$, $R^2 = H$; 9: $R^1 = CO_2R$, $R^2 = NR_2$.

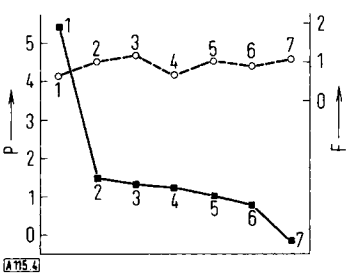
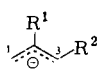


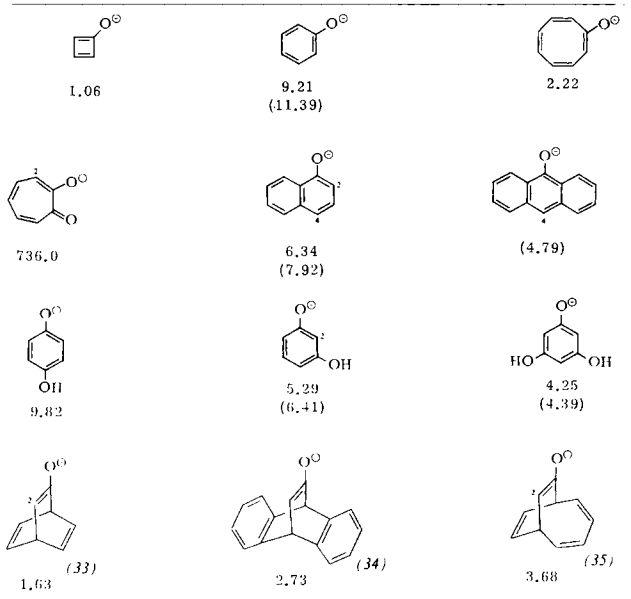
Fig. 4. Comparison of the polarity index $P = l_1/l_3$ (——) and the "orbital index" $F = c^2_{3,\,HOMO}/c^2_{1,\,HOMO}$ (– – –). The indices compared are those for substituted allyl anions of the type



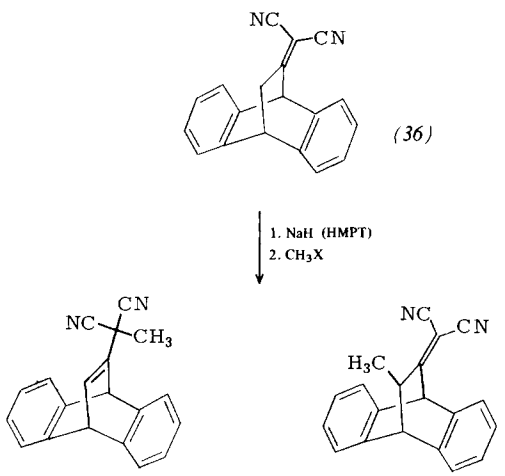
1: $R^1 = CO_2R$, $R^2 = NR_2$; 2: $R^1 = H$, $R^2 = NR_2$; 3: $R^1 = R^2 = NR_2$; 4: $R^1 = NR_2$, $R^2 = CO_2R$; 5: $R^1 = R^2 = H$; 6: $R^1 = H$, $R^2 = CO_2R$; 7: $R^1 = R^2 = CO_2R$.

It is remarkable that the anion *(35)* possesses a higher polarity index than the anions *(33)* and *(34)*. This is in accord with the finding that *(35)* is only *O*-methylated (Na salt + dimethyl sulfate in DMSO)[124]. In the case of *(34)*, on the other hand, *C*-methylation predominates (Li salt + dimethyl sulfate in ether; the ion-pair effect may be significant

Table 9. Polarity indices of "aromatic" enolate ions. The values given are $P = I_O/I_{C-2}$ and I_O/I_{C-4} (in parentheses).



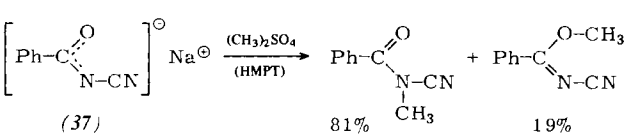
here)[125]. With the Na salt of *(36)*[125], too, methylation proceeds less selectively than is normally found with 1,1-dicyanoallyl anions (see Section 3.1).



X = OSO_3CH_3	95%	5%
X = I	75%	25%

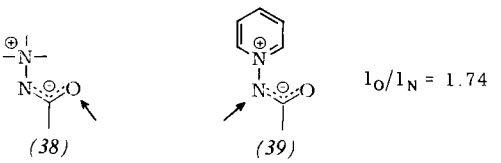
3.5. Amide and Thioamide Anions

Judging by the electronegativities of C, N, and O, the reactions of amide anions would be expected to follow a similar pattern to enamine anions. Thus instead of the *C*-alkylation prevailing with the simple enamine anions, *N*-alkylations should be observed for amide anions. This is indeed the case[126, 126a] when alkali metal salts are employed; silver salts lead to exclusive or partial *O*-alkylation (alkylation of α-pyridone has been studied particularly thoroughly[127]).



(37) 81% 19%

The enhancement of polarity by acceptor substituents at the N atom is manifested on methylation of *(37)*[38] and alkylations of the zwitterions *(38)*[128, 129] [the reasons for the deviating behavior of the pyridinium derivatives *(39)*[128] are unclear].

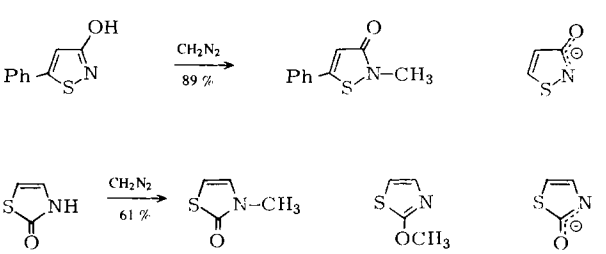


The polarity indices of amide anions in lactam systems show wide variation (cf. Table 10). However, no comparative studies of alkylations and acylations under standard conditions have been reported. That the polarity indices in Table 10 point in the right direction is shown, *inter alia*, by the almost invariable *N*-alkylation of imide anions of type *(40)* (formation of an *O*-substituted derivative on reaction of Ag maleimide with 1-bromoadamantane in benzene[130] is an exception), as against the pronounced tendency of cyclic hydrazide anions of type *(41)* to undergo *O*-alkylation and *O*-acylation[131].

Table 10. Polarity indices $P = I_O/I_N$ of some amide anions.

	I_O	I_N	P
(40)	−0.540	−0.502	1.076
	−0.720	−0.517	1.393
	−0.625	−0.375	1.666
	−0.743	−0.407	1.826
	−0.799	−0.291	2.746
	−0.799	−0.269	2.970
(41)	−0.809	−0.214	3.780
	−0.820	−0.191	4.293

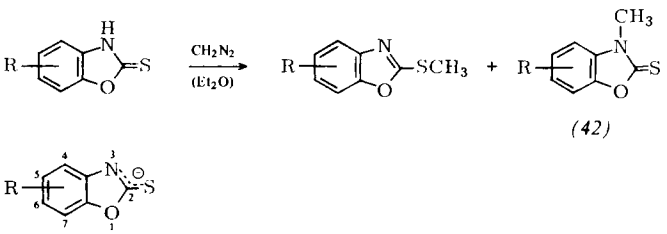
The differences in reaction conditions also preclude a general correlation of the reaction between amide systems and diazomethane[132] with polarity indices. Nevertheless, notable relationships between the course of methylation and polarity can be detected with closely related compounds, *e.g.* 3-isothiazolone and 2-thiazolone (see Scheme 11); concerning the *N*-benzylation of 3-isothiazolone cf. ref. [135]).



Scheme 11. Methylation of 5-phenyl-3-isothiazolol (for the anion $P = I_O/I_N = 1.98$; $I_O = -0.737$ and $I_N = -0.373$) [133] and methylation of 2-thiazolone (for the anion $P = I_O/I_N = 2.30$; $I_O = -0.724$ and $I_N = -0.322$) [134].

Although 7-azabicyclo[4.2.2]deca-2,4,9-trien-8-one is to be regarded as the N-analog of *(35)* (Table 9), it is only *N*-methylated (NaH, DMF, dimethyl sulfate)[136].

Thioamide anions are usually *S*-alkylated[126]. However, in the case of *N*-acylthioamide anions *N*-alkylation also occurs (5-alkylidenerhodanines[137], 2-thio- and 2,4-dithiohydantoins[138], 2-thio-6-azauracil[139], 4-thioxothiazolo-[3,2-*a*]-*s*-triazin-2-one[140]). The relation between *N*-methylation and increasing polarity index of thioamide anions is evident from Table 11.



(42)

Table 11. Methylation of substituted 3*H*-benzoxazole-2-thiones [141]. Yields of NCH_3 derivative are given *(42)*. $P = I_N/I_S$.

R	I_S	I_N	P	*(42)* Yield [%]
H	−0.477	−0.537	1.126	3.5
5-NO_2	−0.366	−0.520	1.421	6.1
7-NO_2	−0.355	−0.511	1.439	8.0
6-NO_2	−0.209	−0.345	1.651	17.6
4-NO_2	−0.199	−0.332	1.688	64.7

3.6. Other Anions

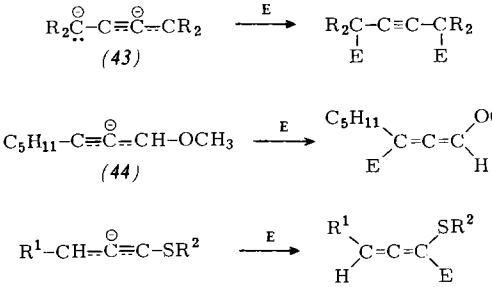
A number of ambifunctional anions are summarized in Table 12. Comparing the reactions of those anions which contain the same reactive sites (O/C and O/N) once again reveals the relation between polarity and selectivity (the arrows symbolize product formation). Oxime anions[142]—nitrone

Table 12. Polarity indices of some ambifunctional anions. $P = I_O/I_X$.

Anion		I_O	I_X	P
	Amide	−0.720	−0.517	1.39
	Enol	−0.785	−0.301	2.61
	Nitroalkane	−0.805	−0.037	21.76
	Nitrosamine	−0.677	−0.384	1.76
	Oxime	−0.778	−0.111	7.01
	Nitramine	−0.703	−0.379	1.85

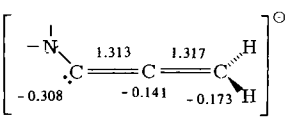
formation[143–145] is excluded from our present discussion since only reactions at the sites X and Y of anions of type *(2)* are being considered—and especially nitroalkane anions[146] have much greater polarity indices than enolate ions[146], and it is therefore hardly surprising that oxime anions are exclusively *O*-alkylated. Hydrazone anions (see Section 3.3) are accordingly 1-alkylated[147–154]. In contrast, amide anions, nitrosamine anions[155–157], and nitramine anions[158–160] exhibit relatively low polarity indices of similar size, and *N*-alkylation accordingly predominates.

It might be expected that the substituent effects observed with the anions *(2)* will also occur with the anions *(4)*. The simplest case is that of the propargyl anions. The reactions of *(43)*[162], *(44)*[162–165], and *(45)*[166,167] correspond to the pattern already established for the allyl anions (see Section 3.1).



(43) *(44)*

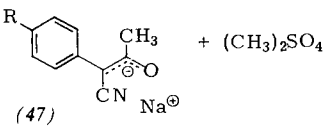
The situation is different in the case of the anions of ynamines[168] and alkoxyallenes[169]. MINDO/3 calculations have shown that such anions have structures resembling *(46)*, *i.e.* are not planar, and react like vinyl anions. (The bond lengths [Å] are given above the formula, and charge densities below.)



(46)

Alkynethiolates[170] behave in similar manner to enethiolates on alkylation; with lithium phenylethynolate[171] the tendency to react at the C atom appears even more pronounced than with enolate ions.

The concept of allopolarization is based upon the assumption of a relatively early transition state. Although this assumption is problematic, the reactivity generally has no influence on the selectivity (see Table 2). However, if anions bearing different kinds of substituents happen to have the same polarity, the reactivity can decide the selectivity. Table 13 illustrates such a case[38]. The anions[47] with R=H and R=Cl have the same polarity index but different reactivity. The larger



(47)

Table 13. Influence of the reactivity on the selectivity in compounds having equal polarity indices. $P = I_O/I_C$; the enol/ketone ratio given refers to the starting material.

R	P	Q_O/Q_C	ε_{HOMO} [β]	Enol/Ketone
CH_3	3.341	1.8	0.307	0.67
H	3.328	1.2	0.346	0.98
Cl	3.327	2.4	0.381	3.20

yield of enol ether in the case of *(47)*, R=Cl, can be explained by the "later" appearance of the transition state than for

(47), R = H, so that the bonding in the product also affects the selectivity [the greater enol content of the starting material suggests that for *(47)*, R = Cl, the enol ether is more stable than in the other two cases].

4. Conclusion

With regard to synthetic strategy the following summary rules can be drawn up for the reactions of ambifunctional anions:

1) By starting from the known reactions of an ambifunctional parent system of type *(2)* the "selectivity factor" $S_f = \log Q_X/Q_Y$ is established (see Scheme 4). The influence exerted by a perturbation due to substituents on the parent system is then examined. The change in the "polarity index" $P = l_X/l_Y$ is taken as a measure of the perturbation.

An increase (decrease) in P indicates enhancement (diminution) of charge control. The result is an increased tendency to undergo reaction at that site (X or Y) of the anion which bears the greater (smaller) partial negative charge.

2) The statement of expected selectivity in the reactions of a (substituted) anion, as derived according to 1), has to be modified in special cases (equal polarity of two anions) by taking into account the change in reactivity due to the perturbation (early/late transition state).

3) Polarity and reactivity of the electrophilic reactants according to 1) and 2) are included.

4) The solvent effect is taken into consideration (empirical solvent parameter).

The rules of the allopolarization concept cannot be applied to reactions in which π-complexes or ion pairs occur as intermediates since their subsequent reactions cannot be directly deduced from the properties of the starting materials. Formation of such intermediates is to be expected above all in reactions of cyclic π-systems. Examples are the reactions of pyrrole- and imidazole anions to form heterofulvalenes[172] and the acylation of 5-oxazolones in the presence of pyridine[87, 173].

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Hydrozirconation: A New Transition Metal Reagent for Organic Synthesis

New synthetic methods (16)

By Jeffrey Schwartz and Jay A. Labinger[*]

Hydrozirconation has recently been developed as a procedure for functionalizing alkenes, alkynes, and 1,3-dienes *via* organozirconium(IV) intermediates. These intermediates react with a variety of electrophilic reagents to give organic products in high yield. Mechanisms of reactions involved in these sequences are discussed.

1. Introduction

Because of the scope of reactions found in transition metal organic chemistry, there is much current interest in the development of transition metal complexes as reagents for organic synthesis. Transition metal hydrides constitute one class of compounds presently under study, since by selective hydrometalation readily available starting materials, olefins or acetylenes, can be converted specifically into reactive σ-bonded organometallic intermediates, at least in theory; upon C—M cleavage these intermediates give the desired organic product. Hydrides of main group elements (*e.g.*, boron[1], aluminum[2], or tin[3]) have become commonly used stoichiometric reagents for accomplishing this type of synthetic transformation, and transition metal hydrides find use as catalysts for reactions of unsaturated hydrocarbons such as hydrogenation, hydroformylation, hydrosilation, and isomerization[4].

To develop transition metal hydrides as useful reagents of general applicability, it is necessary to find such complexes which will react with ordinary "unactivated"[**] alkenes or alkynes to give alkyl- or alkenyl-metal derivatives in high yield. The presence of electron-withdrawing substituents on the unsaturated organic molecule seems to favor this reaction. For this reason the study of the formation of transition metal-carbon σ-bonds by β-hydride addition to unsaturated organic molecules has heretofore centered around the chemistry of transition metal hydrides and olefins or acetylenes containing electron-withdrawing substituents such as tetrafluoroethylene[5,6], hexafluoro-2-butyne[7], dimethyl acetylenedicarboxylate[8], acrylonitrile[7,9], and fumaronitrile[7]. Unfortunately, whereas these substrates do provide important mechanistic information, they are not generally useful precursors of desired organic products.

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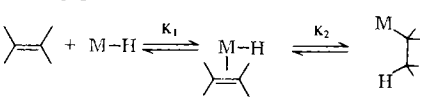
[**] By "unactivated" we mean acetylenes or olefins which are substituted with alkyl or proton substituents only.

The conversion of an unactivated alkene or alkyne into a transition metal alkyl or alkenyl involves two steps (Scheme 1):

1) Coordination of the olefin or acetylene to the transition metal atom;
2) "β-M-H addition" to the coordinated unsaturated molecule.

Scheme 1.



For a variety of transition metal complexes the magnitude of the equilibrium constant K_1 has been found[10] to depend on the number and size of alkyl substituents attached to the double bond; as these increase, K_1 decreases rapidly. β-Hydride addition or elimination in transition metal complexes (K_2) has been studied in numerous cases[6,11–14], and *Hoffmann* has recently proposed[15] that the position for this equilibrium (K_2) should depend on the availability of electron density on the metal to stabilize the alkene complex; its increase favors the hydrido-alkene species. Similar arguments are applicable to alkyne chemistry.

The reaction between ethylene and certain transition metal hydrides which are catalytically active can result in the formation of an isolable ethyl derivative[6,16–20]. Although alkyl-metal derivatives cannot usually be observed in reactions between higher alkenes and transition metal hydrides used as homogeneous catalysts, there is evidence for their formation as intermediates[6,19]. Even though the concentration of an alkyl-transition metal compound thus formed is too low to be detected directly, several types of catalytic sequences involving such intermediates are known. In catalytic hydrogenation, for example, even though K_1 and K_2 can be relatively unfavorable, the reagent that ultimately effects C—M bond cleavage in the intermediary alkylmetal species, *viz.* H_2, does not destroy the metal hydride catalyst; it can react *reversibly* with H_2 to give a metal trihydride[4,21]. A different situation exists when the cleavage reagent chosen is not H_2 (or is any other species that reacts irreversibly with the metal hydride). Here,

consumption of the metal hydride reagent can occur to give a low yield of desired product unless

- a) The alkyl compound is disfavored relative to either hydride species at equilibrium (Scheme 1), but the cleavage reagent attacks it preferentially;
- b) β-hydride addition is fostered by attack of the cleavage reagent on a metal hydride species;
- c) the alkyl compound is favored relative to both hydride species at equilibrium (Scheme 1) and the cleavage reagent can react with any of these complexes with comparable facility.

Hydrozirconation, a process permitting the selective and high-yield conversion of unactivated alkenes and alkynes into a variety of types of organic products *via* isolable σ-bonded organozirconium intermediates, was developed as a result both of the mechanistic considerations discussed above and of synthetic studies using hydrides of various other transition metals. This evolution is traced in brief below.

2. Hydroacylation

Preliminary studies indicated practical limitations for sequences involving condition (a) described in Section 1. Ethylene can be converted into an ethyl ketone *via* an ethylrhodium or ethylcobalt complex generated by reaction with $HRh(CO)L_3$ or $HCo(N_2)L_3$ ($L=PPh_3$)[22]. In this sequence ketone is formed by oxidative addition of acyl halide to the alkyl-transition metal intermediate followed by reductive elimination of the product[23,24]. However, the use of higher olefins results in diminished yield of ketone. Meager success with these substrates can be attributed to unfavorable factors associated with the equilibrium constant K_1 (Scheme 1) and the observation that many acyl halides react irreversibly with $HRh(CO)L_3$ or $HCo(N_2)L_3$ to give halometal complexes. Although the equilibrium concentration of alkyl is not high even for ethylene, the reaction of ethylrhodium or ethylcobalt is faster than that of the hydride with acyl halide; hence for ethylene the concentration of alkylmetal is sufficiently large to give yields of ketone as high as 86% (based on starting metal hydride). With long chain alkyl substituents on the double bond the concentration of the alkylmetal drops so that most of the starting hydride is consumed by the acyl chloride.

Scheme 2.

$$RCH{=}CH_2 + MH \xrightarrow{R'\overset{O}{\overset{\|}{C}}Cl} RCH_2CH_2\overset{O}{\overset{\|}{C}}{-}R'$$

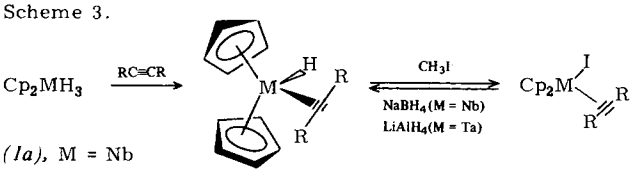
MH = $HRh(CO)L_3$, $HCo(N_2)L_3$ (L = PPh_3)

R	R'	Yield [%] (M = Rh)	(M = Co)
H	C_6H_5	86	75
$CH_3CH_2CH_2$	CH_3	2	20

3. Alkenyl-tantalum(III) and -niobium(III) Complexes

Parshall et al. have reported[20] that Cp_2NbH_3 *(1a)* ($Cp=\eta^5$—C_5H_5) coordinates ethylene with loss of H_2 to give $Cp_2NbH(C_2H_4)$ *(2)* and that further treatment of *(2)* with ethylene results in the formation of an isolable ethylniobium(III) species. Study of the reaction between Cp_2MH_3 *(1)* (M = Nb, Ta) and dialkylacetylenes was initiated in light of these results[25,26]. Few complexes of dialkyl-substituted acetylenes are known[27,28]; however, it was found that treatment of *(1)* in benzene with such alkynes gave in high yield the first known examples of hydrido-alkyne complexes, $Cp_2MH(C_2R_2)$ *(3)* (Scheme 3), compounds which can be used as models to explain the selectivity of the hydrozirconation process (see below). These compounds *(3)* (M = Nb) could not be prepared by displacement of the phosphane ligand from $Cp_2NbH(L)$[29].

Scheme 3.



(1a), M = Nb
(1b), M = Ta

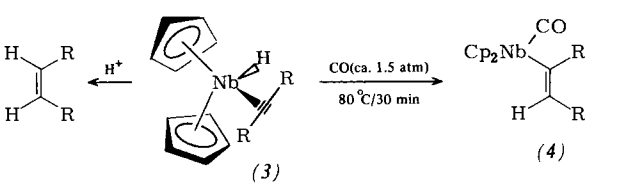
(3)

Crystallographic studies[30] on $Cp_2Nb(C_2H_4)C_2H_5$ indicate that Nb is pseudotetrahedrally coordinated and that the two carbon atoms of the ethylene ligand lie in a plane which also contains the niobium atom and the α-carbon atom of the ethyl chain. NMR evidence obtained for the related species *(3)* indicates that the acetylene unit in these complexes is deployed in the same fashion: the hydrido ligand, the metal atom, and both carbons of the acetylenic unit all lie in one plane. In this geometry one substituent on the triple bond is in a relatively uncrowded environment near the sterically small hydrido ligand while the other substituent on the triple bond resides in a more congested surrounding near the two cyclopentadienyl rings (Scheme 3). Two consequences of this mode of coordination are notable:

1) Coordination of a symmetrically substituted acetylene renders the two ends of the alkyne ligand non-equivalent;

2) coordination of an unsymmetrically substituted acetylene gives rise to two isomers which differ only in the orientation of the alkyne ligand in the plane containing the M—H bond. If the substituents on the triple bond differ in steric size, that isomer should predominate in which the largest substituent lies nearer the small hydrido ligand.

Scheme 4.

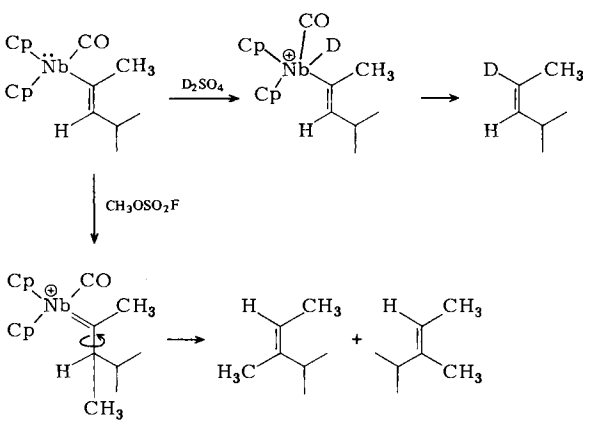


(3) *(4)*

Protonation of *(3)* (M = Nb, Ta) yields *cis* olefins as does its reaction with H_2[26] [see condition (b) in Section 1]. Treatment of *(3)* (M = Nb) with CO as shown in Scheme 4 converts it into the alkenylcarbonyl species *(4)*. This σ-bonded organometallic species is formed with (C=C) *cis* stereochemistry[8] by β-Nb—H addition to the triple bond. It is interesting to note that for 4-methyl-2-pentyne greater regioselectivity is observed in *(4)* than was found in its precursor *(3)*: quantitative NMR analysis demonstrates that all of *(3)* is converted into *(4)*. This observation can be explained by a process in which the alkyne ligand is free to rotate about the metal-ligand bond axis, as has been demonstrated in another system[31]. Since the steric requirements of the alkenyl ligand

are different from those of the alkyne one, the selectivity displayed by the starting material is different from that shown by the σ-bonded product. Carbon monoxide traps the coordinatively unsaturated alkenyl complex. Note that in both *(3)* and *(4)* a lone pair of electrons is present which is formally associated with the Nb^{III} (d^2) metal center. Such a pair of electrons associated with a metal center can be protonated or alkylated[32,33]. The formation of *cis* olefin upon protonation of *(4)*[25] can be envisioned as proceeding through such a protonation of niobium(III) followed by reductive elimination of olefin from the resulting cationic niobium(V) intermediate (Scheme 5). Labeling studies with D_2SO_4 support the proposed mechanism for protonation: in the olefinic product deuterium replaces the niobium. A parallel synthesis of a trialkyl-substituted olefin from *(4)* was therefore attempted. However, although a trialkyl olefin *is* formed upon treatment of *(4)* with CH_3OSO_2F, the product observed[25] was *not* the one predicted by this mechanism. Rather, a mixture of isomeric olefins was formed. This mixture probably arises from alkylation at the β-carbon of the alkenyl ligand followed by proton migration and reductive elimination of olefin (Scheme 5). The cationic carbene complex intermediate contains a single C—C bond and rotation about this bond prior to proton transfer leads to the *cis-trans* mixture of product observed. This pathway is not unprecedented: *Casey* has shown[34] that deprotonation of a transition metal alkyl carbene complex occurs at the β-carbon to yield a species best described as an alkenyl complex, and that protonation or alkylation of this alkenyl compound also occurs at the β-carbon to regenerate a carbene complex.

Scheme 5.



Cp = η^5-C_5H_5

4. Organozirconium(IV) Chemistry

Results with the niobium(III) and tantalum(III) systems described in Section 3 indicate that the system Cp_2MHX can be used to selectively functionalize unsymmetrically substituted acetylenes. However, with these d^2 metals cleavage of the organometallic intermediate was found to be non-specific. Using a d^0 metal in Cp_2MHX (*e.g.* $M = Zr^{IV}$), specific C—M cleavage as well as specific activation of an olefin or an acetylene could be possible. Arguments described earlier also suggest that for a formally d^0 metal the alkyl complex should predominate over the hydrido (alkene) species at equilibrium (K_2 in Scheme 1).

4.1. Background

A variety of stable zirconium(IV) alkyls have been prepared by conventional alkylation of $ZrCl_4$ with Grignard, lithium, or aluminum reagents[35]. Several of these compounds demonstrate appreciable thermal stability, including tetraneopentylzirconium(IV)[36], tetranorbornylzirconium(IV)[37], and tetra(trimethylsilylmethyl)zirconium(IV)[38]. Tetrabenzylzirconium(IV) is also known[39] and has shown limited use as a hydrogenation catalyst. However, none of these organozirconium compounds has seen extensive use as a reagent in organic synthesis. Alkylchlorobis(cyclopentadienyl)zirconium(IV) complexes have been prepared from Cp_2ZrCl_2 and lithium[40] or Grignard[41] reagents. These compounds have been briefly investigated with regard to NO[40] and SO_2[40] insertion into the C—Zr bond[41,42]; their hydrolytic lability has also been noted[40].

The preparation of alkylzirconium compounds has now been accomplished by reaction of Cp_2ZrHCl with a variety of unsaturated organic molecules. This reaction, named "hydrozirconation", is described in detail below.

4.2. Hydrozirconation

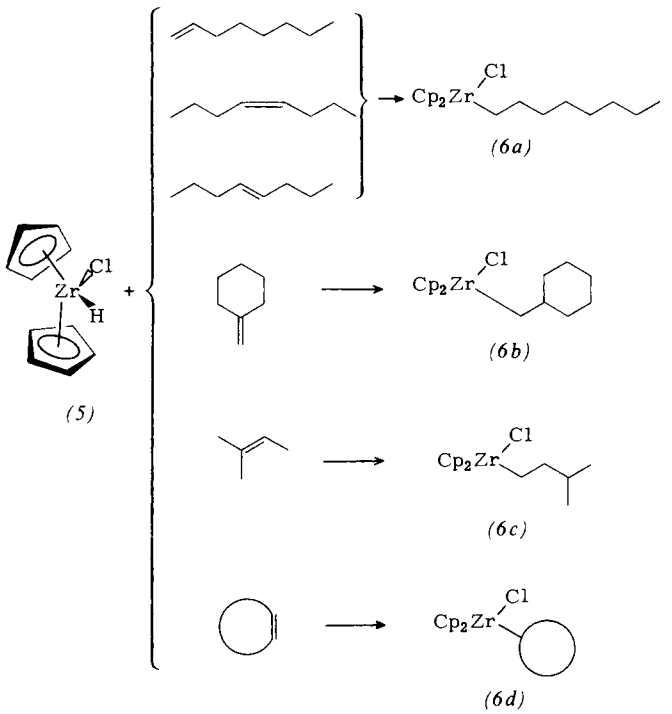
The zirconium hydride $Cp_2Zr(H)Cl$ *(5)* was first prepared by *Wailes et al.*[42] from Cp_2ZrCl_2 and $LiAlH_4$. It is also easily prepared by treatment of the dichloride in tetrahydrofuran with a stoichiometric amount of $NaAlH_2(OR)_2$. Both procedures result in the high yield precipitation of *(5)*[43].

4.2.1. Hydrozirconation of Alkenes

Wailes briefly studied the reactions of *(5)* with several olefins[42]; the resulting alkyl complexes were not identified. This hydride was later found[43] to react under mild conditions with a variety of olefins to generate isolable alkylzirconium(IV) complexes $Cp_2Zr(R)Cl$ *(6)*. Hydrozirconation of olefins proceeds to place the zirconium moiety at the sterically least hindered position of the olefin chain as a whole[43] (cf. Scheme 6). Formation of this product involves either the regiospecific addition of Zr—H to a terminal double bond or Zr—H addition to an internal double bond followed by rapid rearrangement *via* Zr—H elimination and readdition to place the metal in each case at the less hindered position of the alkyl chain. In contrast to *(5)* other transition metal hydrides are known[19] to catalyze the conversion of α-olefins into thermodynamically more favored isomers having an internal double bond but do not form isolable alkyl complexes. Although this observation represents the first instance in which a stable alkylzirconium compound is formed by rearrangement of an unisolated precursor, the migration of a Zr moiety from a secondary carbon to the terminal position of an internally functionalized starting material is not totally unprecedented. Thus Zr^{IV} and Ti^{IV} salts are known to catalyze the isomerization of secondary Grignard[44] and aluminum[45] reagents to give primary ones and these isomerization procedures most likely involve the intermediacy of Zr^{IV} or Ti^{IV} alkyl derivatives. Isomerization here too probably occurs through reversible β-hydride elimination and readdition. In the case of alkylzirconium(IV) complexes prepared from *(5)*, the migration of these metallic moieties proceeds rapidly at room temperature in contrast to analogous organoboron[46] or -aluminum com-

pounds[47], which rearrange only slowly at elevated temperature.

Scheme 6.

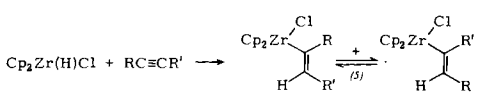


Relative rates[43] for hydrozirconation of alkenes with *(5)* (at room temperature) are α-olefin > *cis* internal olefin ≈ *trans* internal olefin > exocyclically functionalized olefin > cyclic olefin; terminal olefin > disubstituted olefin > trisubstituted olefin. Tetrasubstituted olefins such as tetramethylethylene fail to react with the hydride after many hours at room temperature, as do trisubstituted cyclic olefins such as 1-methylcyclohexene. Competition studies indicate that an α-olefin (*e.g.*, 1-octene) reacts about seventy times faster than do either *cis* or *trans* disubstituted olefins (*e.g.*, 2-octene).

4.2.2. Hydrozirconation of Alkynes

Wailes et al. have reported[48] that hydrozirconation of terminal alkynes proceeds with (C=C) *cis* stereochemistry to place the metal at the terminal carbon atom. Hydrozirconation of various unsymmetrically disubstituted acetylenes occurs[49] readily to give mixtures of alkenylzirconium derivatives in which the relative steric bulk of the alkyl substituents on the C≡C bond dictates the preferred direction of Zr—H *cis*-β addition. The composition of such a mixture of vinylzirconium(IV) compounds does not appreciably change as a function of time if *(5)* is not present in excess. However, with added *(5)*, isomerization to an equilibrium mixture takes place at room temperature (Table 1). The composition of this mixture displays higher regioselectivity than that observed in hydroboration of unsymmetrical acetylenes with hindered boranes[50]. In no case were products derived from allylic rearrangements detected[51].

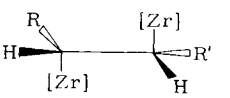
Table 1. Hydrozirconation of unsymmetrically disubstituted acetylenes.



Alkyne R	Alkyne R'	Product ratio (*A*:*B*) [a] initially observed	Product ratio (*A*:*B*) [a] after treatment with *(5)*
H	n-C_4H_9	>98:2	
CH_3	CH_3CH_2	55:45	89:11
CH_3	$CH_3CH_2CH_2$	69:31	91:9
CH_3	$(CH_3)_2CHCH_2$	55:45	>95:<5
CH_3	$(CH_3)_2CH$	84:16	>98:<2
CH_3	$(CH_3)_3C$	>98:2	

[a] Determined by NMR analysis [49].

Isomerization probably occurs through the intermediacy of doubly metalated alkyl derivatives *(7a)* analogous to the one isolated *(7b)*[48] from the reaction between *(5)* and diphenylacetylene. Since metal hydride addition and elimination both occur stereospecifically *cis*, there is no loss of (C=C) stereochemistry in the isomerization process.

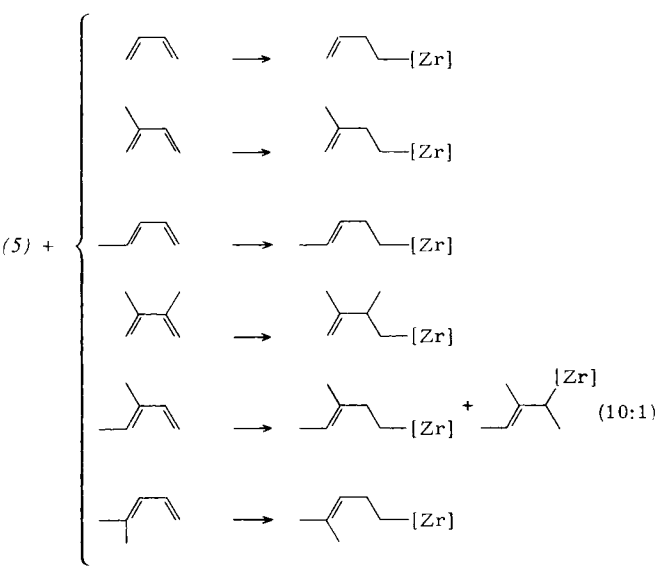


(7a), R, R' = Alkyl
(7b), R = R' = Phenyl

4.2.3. Hydrozirconation of 1,3-Dienes

While the overall mode of addition of *(5)* to alkenes and alkynes parallels reactions known for several main group or transition metal hydrides, the course of addition of *(5)* to 1,3-dienes is significantly different. In contrast to boron-[52] or aluminum hydrides[53], which often doubly metalate 1,3-dienes or give a mixture of products, or to most transition metal hydrides which undergo 1,4- or 1,2-addition to yield allylic complexes[54], *(5)* reacts with a variety of 1,3-dienes by 1,2-addition to the sterically less hindered double bond to give γ,δ-unsaturated alkyl complexes in high yield (see Scheme 7)[55]. However, 2,4-dienes do not behave analogously. Rather, they react with three equivalents of *(5)* (as confirmed by [D]-labeling studies) to give *saturated* alkylzirconium compounds[61]. The mechanism of this unusual transformation has not yet been established.

Scheme 7.



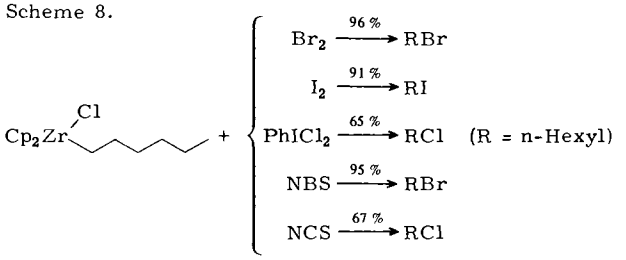
[Zr] = $(\mu^5\text{-}C_5H_5)_2ZrCl$

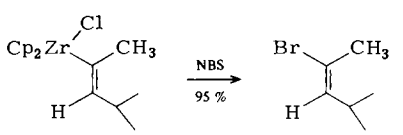
4.3. Cleavage of the Carbon-Zirconium Bond

4.3.1. Alkyl and Alkenyl Halides

Electrophilic halogenation reagents (*e.g.*, Br_2, I_2, *N*-bromo- or *N*-chloro-succinimide, or iodobenzene dichloride) react with alkyl-[43,55] or alkenylzirconium(IV)[49] complexes to yield the corresponding organic halides (Scheme 8). In contrast to reactions involving electrophilic attack upon alkenylniobium(III) complexes[25] (see Section 3), the isomeric composition of the vinyl halide product closely duplicates that of its alkenylzirconium precursor and no *cis-trans* isomerization in the vinyl halide obtained is detectable.

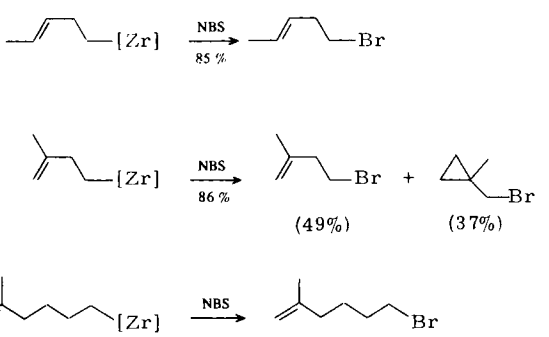
Scheme 8.





For γ,δ-unsaturated alkylzirconium(IV) complexes[55] yet another mode of carbon-metal bond cleavage is also possible. For the compounds shown in which there is a methyl group on the 3-position of the original 1,3-diene, electrophilic attack on the remote double bond can occur to eventually generate (1-methylcyclopropyl)methyl halide (Scheme 9). Noteworthy here is the observation that only properly alkyl-substituted γ,δ-unsaturated alkylzirconium precursors undergo cyclization; the alkyl derivative prepared from 2-methyl-1,5-hexadiene reacts with NBS to yield only the acyclic compound, 6-bromo-2-methylhexene.

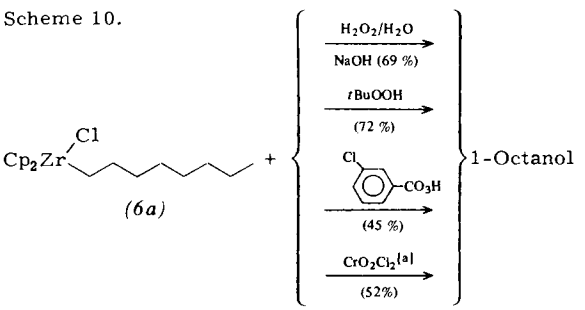
Scheme 9.

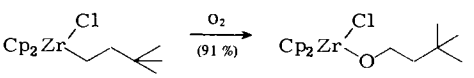


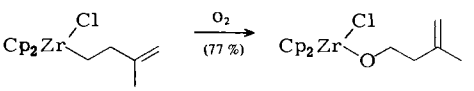
4.3.2. Alcohols[56]

Oxidation of the alkyl carbon-zirconium bond can be effected by O_2 or by various electrophilic oxidizing reagents such as hydrogen peroxide, *tert*-butyl hydroperoxide, *m*-chloroperbenzoic acid, or chromyl chloride. When protic reagents are used, reaction with the alkylzirconium species yields the corresponding alcohol directly. For O_2 or chromyl chloride an alkoxide species is produced which on hydrolysis gives the alcohol. Reaction with chromyl chloride is complicated by the formation of some by-product alkyl chloride. The reaction of alkylzirconium(IV) complexes with O_2 is very slow and requires several hours to attain completion. γ,δ-Unsaturated alkyl derivatives can be oxidized using O_2 to give γ,δ-unsaturated alcohols (Scheme 10). However, attempts to oxidize alkenylzirconium(IV) compounds to give ketones (after hydrolysis) have met with only moderate success; oxidation with O_2 fails completely and only a low yield of ketone is produced with *tert*-butyl hydroperoxide.

Scheme 10.





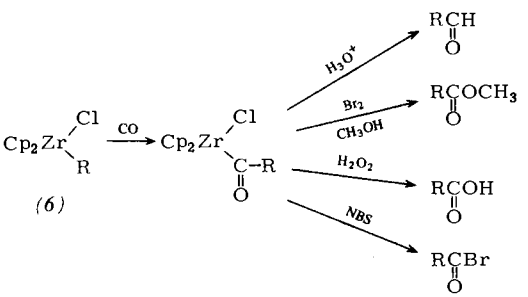


[a] some 1-chlorooctane is also formed.

4.3.3. Insertion Reactions

Carbon monoxide does not insert into the benzyl-zirconium bond of $Cp_2Zr(CH_2C_6H_5)_2$ even under forcing reaction conditions (100°C, 40 atm)[57], and $Cp_2Zr(CH_3)_2$ reacts with CO under pressure (20°C, 40—80 atm) to give an unstable acyl-alkyl species which rapidly loses CO at 1 atm[58]. In contrast to these, CO undergoes clean and high-yield insertion (20°C, 1.5 atm) into the C—Zr bond of many alkyl, alkenyl, or γ,δ-unsaturated alkylzirconium(IV) complexes to generate isolable acylzirconium(IV) species which do not lose CO even under vacuum[59]. Relative rates for CO insertion[60] into the C—Zr bond depend on the nature of the organic substituent: cyclohexyl > *n*-alkyl ≈ alkenyl. These acyls can in turn be converted, depending on subsequent procedures, into aldehydes, carboxylic acids, esters, or acyl halides (Scheme 11). An aldehyde is produced by hydrolysis of the RC(O)—Zr bond with dilute aqueous acid. Treatment of the zirconium acyl with

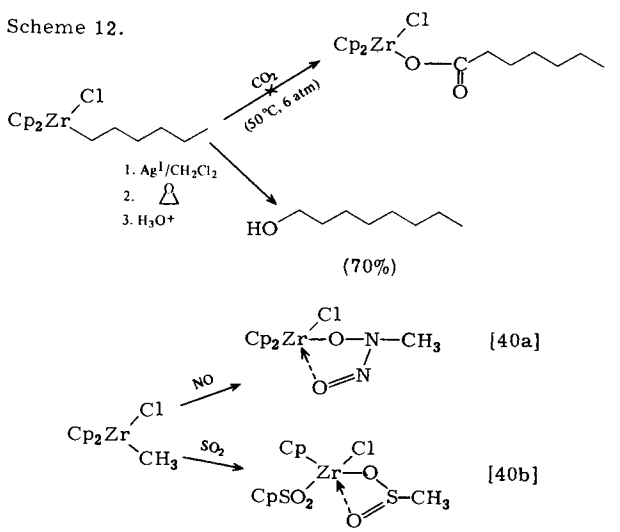
Scheme 11.



NBS gives the acyl bromide. The acyl-zirconium bond can be cleaved by other oxidative procedures as well. Reaction with aqueous H_2O_2 followed by acidification gives the carboxylic acid, and with Br_2 in methanol yields the methyl ester.

Alkylchlorobis(cyclopentadienyl)zirconium(IV) complexes have not been observed to react with carbon dioxide[40, 61] in contrast to tetrabenzylzirconium(IV)[62], which undergoes facile reaction with CO_2 in the molar ratio 1:2. Ethylene oxide inserts slowly into the C—Zr bond of linear alkylzirconium(IV) complexes. This reaction is facilitated by treatment of the organometallic compound with Ag^I in CH_2Cl_2 solution prior to addition of the ethylene oxide. Nitric oxide[40] and sulfur dioxide[40] react with Cp_2ZrMe_2 to form insertion products comprising two equivalents of the electrophilic molecule.

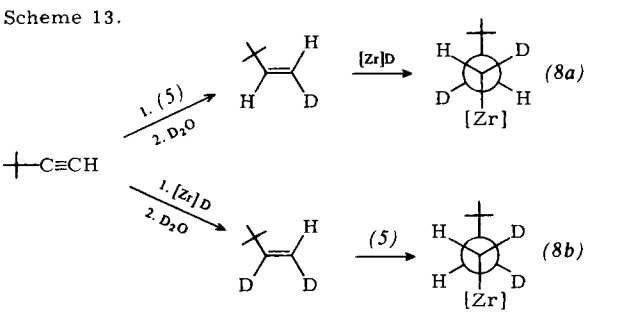
Scheme 12.



4.3.4. Mechanism of C—Zr Bond Cleavage in *(6)*

The mechanism of C—Zr bond cleavage in compounds prepared by hydrozirconation [*(6)*] has been studied[63] by determining the stereochemistry of these processes, employing the NMR technique developed by *Whitesides et al.*[64]. Diastereomerically pure dideuterated 3,3-dimethylbutylzirconium(IV) complexes *(8a)* and *(8b)* were prepared by successive hydrozirconation sequences as shown in Scheme 13. Treatment of 3,3-dimethyl-1-butyne with *(5)* yields the alkenyl derivative as shown, which with dilute aqueous D_2SO_4 gives the olefin indicated (no scrambling of the D label was detectable by NMR). Treatment of this olefin with $Cp_2Zr(D)Cl$ (prepared from Cp_2ZrCl_2 and $LiAlD_4$ in THF) gives the *erythro* alkyl derivative *(8a)* directly; formation of this diastereomer proves that Zr-H addition to an olefin proceeds stereospecifically *cis*.

Scheme 13.



[Zr] = $(\eta^5\text{-}C_5H_5)_2ZrCl$

Cleavage of an alkyl-transition metal bond by bromine proceeding with retention of configuration at carbon has been observed[64] when the metal atom can undergo oxidative addition. Cleavage of the C—M bond by Br_2 with inversion of configuration at carbon has been noted as well[64, 65], and has been interpreted in terms of initial oxidation of the metal complex followed by nucleophilic attack at carbon (with inversion) by Br^- to give the alkyl bromide. Reaction of bromine with *(8a)* or *(8b)* gives the alkyl bromide with retention of configuration at carbon. In the complexes *(8a)* or *(8b)* the metal is formally d^0: hence oxidative addition is not expected and further oxidation will be extremely difficult. A closed transition state such as that proposed for halogenation of organomercurials[66] reasonably accounts for retention at carbon as observed for electrophilic carbon-metal bond cleavage in these alkyl zirconium derivatives (see Fig. 1). Here the electrophilic reagent coordinates to zirconium by donation of a pair of electrons to its vacant low-lying orbital[67], facilitating frontside attack on the C—Zr bond.

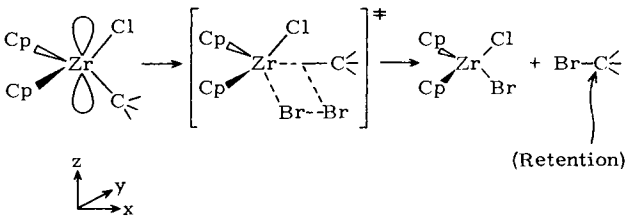


Fig. 1. Probable mechanism of C—Zr bond cleavage, for instance by Br_2.

Carbon monoxide inserts into the C—Zr bond with retention at carbon[63] as has been observed for all other alkyl-transition metal systems studied thus far[64]. Sulfur dioxide also inserts into the C—Zr bond with retention of stereochemistry[63]. It has been reported[40] that $Cp_2Zr(Cl)CH_3$ adds *two* equivalents of SO_2 to give an insoluble product. However, careful addition of *one* equivalent of SO_2 to a solution of *(8a)* or *(8b)* gives a monoinsertion product formulated[63] as $Cp_2Zr(Cl)[O_2S—CHD—CHD—C(CH_3)_3]$ with retention of stereochemistry. This result is in contrast to those[64, 68] obtained for other alkyl-transition metal compounds in which SO_2 insertion proceeds with inversion of configuration at carbon. Nitric oxide also causes electrophilic cleavage of the C—Zr bond with retention of configuration to give the *N*-nitrosylhydroxylamine compound[40]. Electrophilic oxygen reagents such as H_2O_2 or *tert*-C_4H_9OOH transform *(8a)* or *(8b)* into the alcohol with retention of configuration at carbon. These processes too can be accommodated by the closed transition state shown in Figure 1. The postulate that a nucleophilic interaction between the attacking electrophilic molecule and the Zr atom is necessary to effect C—Zr cleavage is supported by the observation that whereas poorly electrophilic (yet mildly nucleophilic) CO readily inserts into the C—Zr bond, the stronger electrophile (but poorer nucleophile) CO_2 does not react with *(6)* even under more stringent conditions.

Treatment of *(6)* with O_2 also gives the corresponding Zr alkoxide[56]. Here stereochemical results indicate that one half of the product is formed with retention at C, while the other half is formed with racemization. One possible mechanism[56] to account for O_2 oxidation is shown in Scheme 14, analogous to those proposed for the autoxidation of Grignard[69] or lithium reagents[70].

Scheme 14.

$$R^*[Zr] + O_2 \longrightarrow R\cdot + \cdot OO[Zr] \longrightarrow ROO[Zr]$$

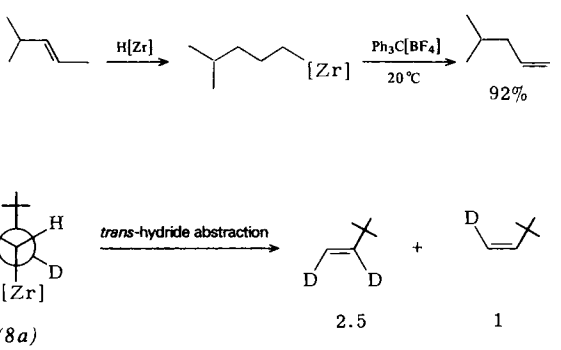
$$ROO[Zr] + R^*[Zr] \longrightarrow RO[Zr] + R^*O[Zr]$$

R^* = chiral alkyl group
R = racemized alkyl group
[Zr] = $(\eta^5\text{-}C_5H_5)_2ZrCl$

4.3.5. Recovery of an Olefin from *(6)*

Hydrozirconation of an alkene having an internal double bond by *(5)* yields the terminally functionalized alkyl complex *(6)* from which the terminal alkene can be obtained. Isomers of the starting olefins can be prepared from rearranged alkylboranes by treatment with a high-boiling terminal olefin and removal by distillation of the desired organic product[71]. This procedure has not yet been successful for *(6)*; the isomerized olefin can be freed neither by treatment with ethylene (even at high temperature and pressure) nor by donor ligands (such as pyridine or alkylphosphanes). However, it is possible to obtain isomerized olefin from *(6)* through β-hydride abstraction as has been observed in iron[72] or tin[73] chemistry. Thus treatment[74] of a solution of the rearranged alkylzirconium derivative with either trityl chloride or trityl tetrafluoroborate in methylene chloride or benzene at room temperature gives the corresponding terminal olefin (Scheme 15). The pattern of D labeling in olefins recovered from *(8a)* indicates that this reaction proceeds through β-hydride abstraction by Ph_3C^+ with *trans* stereochemistry.

Schema 15.



(8a)

4.4. Functional Group Compatibility

Hydride *(5)* can reduce several types of functional groups at a rate competitive with its reaction with an olefin. However, several common and convenient protecting groups have been found to be stable toward the new transition metal reagent. A brief tabulation of functional group reactivity is indicated in Table 2.

It has been reported[75] that Cp_2ZrH_2 reacts with acetone to give $Cp_2Zr[OCH(CH_3)_2]_2$. Hydride *(5)* also reduces free carbonyl groups to Zr alkoxides and nitrile compounds to zirconium imine complexes (similar species have been prepared from the corresponding lithium salts)[76]. These imine salts can be hydrolyzed with dilute aqueous acid to give the corresponding aldehydes[77].

Table 2. Compatibility of functional groups with the hydrozirconation reagent *(5)*; [Zr] = $(\eta^5\text{-}C_5H_5)_2ZrCl$. (An exhaustive study of functional group or protecting group compatibility has not yet been done.)

Reactant	Product with H[Zr]	Protecting group
R—OH	R—O [Zr]	—O—Si$(CH_3)_3$
R—C(O)H	RCH_2OH [a]	
R—C(O)R′	RR′CHOH [a]	
R—C(O)OH	R—CH_2OH [a]	
R—C(O)OR′	R—CH_2OH [a]	—
R—C≡N	R—CHO [a]	—

[a] Upon hydrolysis.

5. Conclusion

The development of *(5)* as a reagent for organic synthesis represents only *one* entry into organozirconium chemistry. For example, sterically congested hydride *(5)* reacts only slowly or not at all with hindered olefins; and, in *(6)*, migration of the metal moiety past a tertiary carbon center is very slow. Therefore, the development of sterically less-crowded zirconium hydrides is a worthwhile aim. Direct alkylation of *(6)* is not yet possible and the means to accomplish this transformation also represents an important goal of future research. Of course, finding new means to effect electrophilic cleavage of the C—Zr bond in *(6)* will continue to be of interest to demonstrate the versatility of these organometallic intermediates.

Apart from its utility as a technique, the development of hydrozirconation illustrates two important points:

1) That synthetically useful transition metal based organometallic reactions can be devised through consideration of organometallic mechanisms.

2) That the introduction of new such procedures will continue to be an exciting aspect of organic synthesis because of the broad scope and high reactivity of organometallic complexes.

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Production of Oil by Hydrogenation of Coal[**]

By K. F. Schlupp and H. Wien[*]

A survey of coal hydrogenation processes revealed that, despite a wealth of experience gathered in Germany up to 1945 some of which served as a basis for further work in the USA, there is at present no process available anywhere in the world for the commercial production of oil from coal. Approaches suitable for further development are the noncatalytic one-step limited hydrogenation and catalytic hydrogenation. Under the most favorable conditions production of oil from coal should become technically feasible some time between the early and mid-1980's. In view of the price of heavy fuel oil the commercial prerequisites for production of synthetic fuel oil from coal are presumably fulfilled only in those countries with low coal prices.

1. Introduction

The energy crisis has shown that the industrial nations are in a vulnerable position owing to their great dependence upon oil imports, and will have to expect further increases in oil prices in the future. Enhanced recourse to coal supplies and liquefaction of this coal to give substitute oil products could alleviate the dependence upon imports and thereby help to ease the situation. Liquefaction of coal also has environmental advantages since the products are largely free from ash and sulfur.

For these reasons the liquefaction of coal is attracting growing interest in countries possessing coal deposits. Much positive efforts will, however, be required to develop the technologies necessary for coal liquefaction to commercial maturity.

2. Market Studies

The potential uses of synthetic fuel oil are determined by the amount of hydrogen added to the coal by the technological process adopted.

Modest addition of hydrogen affords extracts suitable as substitute heavy fuel oil. The synthetic oil could also serve as raw material for products normally obtained from tar or tar pitch, *e.g.* electrodes and binders.

More extensive addition of hydrogen can lead to light and middle distillates well suited as chemical feedstock on account of their aromatic, naphthenic, and aliphatic components.

In the fuel field, coal hydrogenation could provide substitutes for heavy and light fuel oil. The greatest consumers of heavy fuel oil in the Federal Republic of Germany are the heavy and manufacturing industries (58 %) and power stations (24 %).

Commercial production of oil from coal will not become technologically feasible until the early 1980's. A largely constant fuel oil market of about 30 million t/a has been predicted for that period in the Federal Republic. Any significant influence on this market will require production of about 6 to 10 million t/a of oil in large-scale plants, processing about 12 to 20 million t/a of coal.

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Accurate information is not yet available about the constituents of synthetic oil from coal. However, it may be assumed that important raw materials for the chemical industry will be produced from this source.

The oil produced by mild hydrogenation contains about 50 % of a substance resembling coal tar pitch, the rest being oil fractions of various boiling ranges.

The heavy fraction resembling coal tar pitch would be suitable for manufacture of valuable carbon products such as graphite, binding pitches, or special types of coke. Binding pitches are already produced mainly from coal products, while 80 % of the pitch required for producing special cokes is of petrochemical origin.

The oil fractions of the synthetic oil contain aromatic, naphthenic, and aliphatic components. The contents of cyclohexane, benzene, toluene, and xylene, and also of fused aromatics like naphthalene and anthracene, command particular interest for the production of important primary chemicals. Furthermore, tar acids and tar bases, as well as those fractions which may serve as carbon black oils, also possess economic significance.

The present-day contribution of coal chemistry to supplies of raw materials for the chemical industries is low, being estimated as about 10 % of petrochemical feedstock. In view of the expected growth in demand for chemical feedstocks, an additional market of about 1 million t/a of synthetic oil can be envisaged in the chemical industry of the mid-1980's.

3. Product Definition

Product definition for coal liquefaction arises from the objective of producing low-ash and low-sulfur products from coal ranging from heavy fuel oil to middle and light distillates which are stable when stored. Moreover, substitution of heavy fuel oil by the coal-based product should not require extensive adaptation of equipment and plant.

Table 1. Desired properties of oil obtained from coal.

Calorific value	*ca.*	10000 kcal/kg
Density (15 °C)	*ca.*	1.0 kg/dm^3
Flash point		>65 °C
Viscosity at 100 °C	max.	40 cSt
Sulfur content	max.	0.6 wt. %
Ash content	max.	0.1 wt. %

The desired properties of the synthetic oil are listed in Table 1. They largely correspond to those of heavy fuel oil. The values for sulfur and ash content are lower.

4. Survey of Contemporary Processes

4.1. Production of Liquid Products from Coal

Production of liquid products from coal was long accomplished exclusively by thermal treatment. The resulting lignite- and coal tars were the principal raw material of the chemical industry. Meanwhile, products of the petroleum industry have largely replaced tar derivatives.

Table 2. Molecular weights and hydrogen contents of various hydrocarbons.

	g H_2/100 g C	Molecular weight
Coal	6	>5000
Lignite	8	>5000
Petroleum	14	400
Light fuel oil	16	200
Gasoline	17	100
Methane	33	16

As shown in Table 2, high yield conversion of coal into liquid products requires degradation of the high-molecular coal and addition of hydrogen. Without addition of hydrogen, as in purely thermal processes, relatively low yields (5 to 25 % based on the initial amount of coal) of liquid products are obtained.

In 1910, *Bergius*[2] undertook the first industrially oriented investigations, and succeeded in producing petroleum-like products at 400 to 450°C and 150 bar. Experience gained by BASF at Ludwigshafen in the field of ammonia methanol synthesis (high-pressure engineering and catalyst production)[3] permitted development of the Bergius process to technical maturity[4]. The first large-scale experimental plant with a capacity of 100000 t/a of motor gasoline from coal was built at Leuna in 1926. Up till 1945, twelve further plant were commissioned for hydrogenation of tar, lignite, and hard coal, four of them on the territory of the present Federal Republic (Scholven, Gelsenberg, Welheim, and Wesseling). A total of about 15 million t of liquid fuel was produced on the basis of the Bergius process up to 1945. The plant were then either shut down or revamped for hydrogenation of petroleum residues.

Starting in about 1930, the Gewerkschaft Mathias Stinnes attempted to produce low-ash, solid extracts by extraction of coal with suitable solvents[5]. However, such extracts can be degraded to light liquid products only with great difficulty. They are ideally suited to the manufacture of electrodes. A commercial-scale plant producing 30000 t/a of extract was

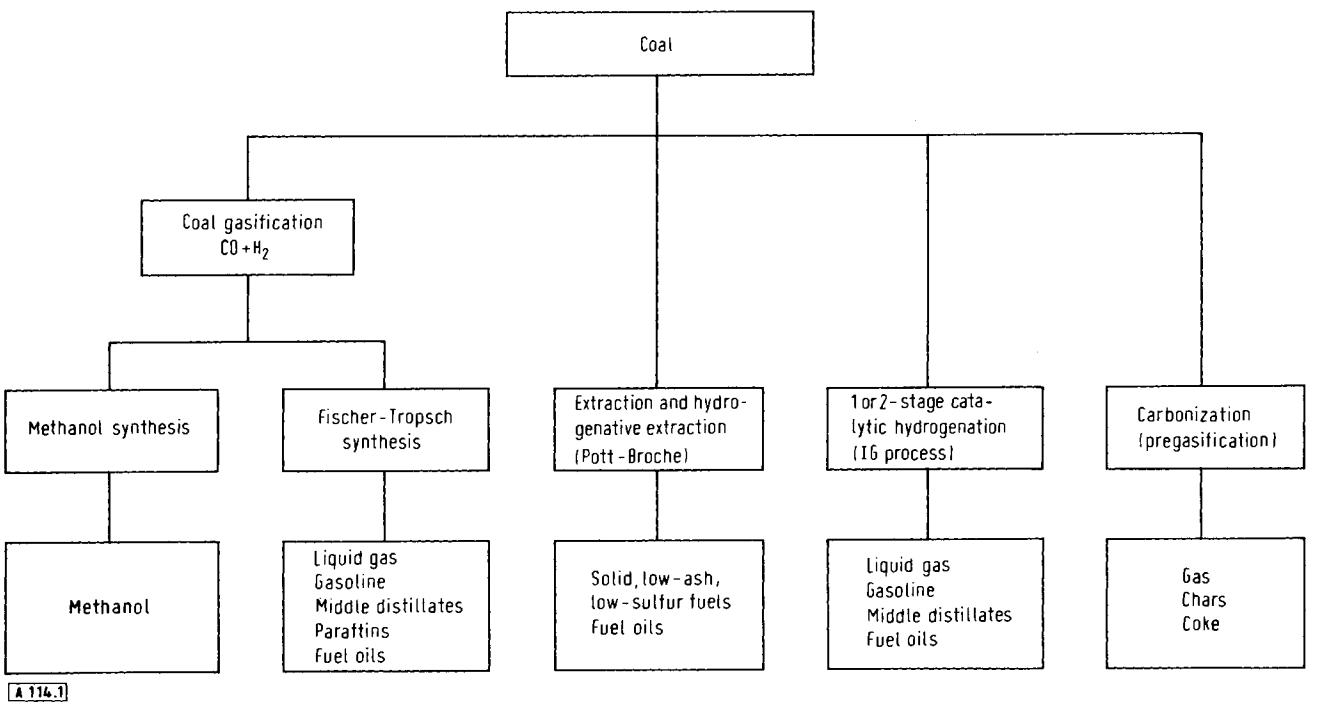

Fig. 1. Processes for liquefaction of coal.

Figure 1 depicts the processes yielding liquid products from coal. Only the carbonization process and the Fischer-Tropsch synthesis are still operating on an industrial scale. Production of methanol is included in the survey since increased efforts have recently been directed toward the use of methanol as a fuel (methyl fuel).

4.2. Historical Development

The first experiments on coal hydrogenation were performed by *Berthelot*[1] as long ago as 1869. They were without industrial significance but did demonstrate the basic feasibility of transforming coal, by addition of hydrogen, into liquid products.

operated by Ruhröl at Bottrop from 1938 to 1944. It was destroyed in the war and was never rebuilt.

In the Pott-Broche process only the solvent serves as hydrogen donor. By introducing a limited direct supply of hydrogen Uhde, and later also IG-Farben, attempted to produce extracts more susceptible to degradation to give liquid hydrocarbons. This Uhde-IG approach was not developed to commercial viability.

The development of coal liquefaction in Germany came to an end in 1945. The reasons were initially the restrictions imposed by the Military Government, and later the lack of

economic interest in the products. Up to about 1963 the remaining high-pressure plant were used for hydrogenation of petroleum residues.

Nevertheless, work was continued on coal liquefaction, above all in the USA and more recently in South Africa, Poland, and Great Britain. Utilizing German know-how, coal liquefaction was introduced in the USA for the production of fuels and chemical feedstocks. The intensity of these efforts lagged and operations were discontinued in the 1950's because the oil industry was marketing increasing quantities of crude oil at low prices. They were taken up anew by coal mining companies in the 1960's. The primary aim was to convert high-sulfur US coal into low-sulfur and low-ash products in order to obtain heating and motor fuels. This work received considerable financial support from the Office of Coal Research and led to the construction of several pilot units. Laboratory experiments were performed on direct conversion of coal into liquid products on fixed catalyst beds. Attempts were also made to operate carbonization processes leading to petroleum-like products in larger pilot plants.

4.3. Individual Processes[6]

4.3.1. The Pott-Broche Process

In the Pott-Broche process finely divided dry coal is extracted at 425 to 440°C and 150 bar with a solvent. Ash and unreacted coal are filtered off. The extract has a softening point of about 220°C and an ash content of <0.2 wt-%. The original solvent was a mixture of tetralin and cresol. Since it had to be rehydrogenated after recovery, later process variants employed a gas-oil fraction of pitch hydrogenation with similar results. Because of the considerable difficulties attending further processing to give lighter products, the extracts were used for manufacturing electrode carbon.

4.3.2. The Uhde-IG Process[4]

The Uhde-IG process is a hydrogenating extraction employing catalysts. The extract obtained at about 450°C and 300 bar has a softening point of 60 to 120°C and an ash content of <0.2 wt-%. Ash and unreacted coal are removed by filtration. The extract can be processed to light distillates in a hydrocracker. This process has so far only been tested on a pilot scale.

4.3.3. The Bergius-IG Process

In the Bergius-IG process coal is converted primarily into distillates in the gasoline boiling range by hydrogenolysis in the presence of catalysts. The process is conducted in two stages. In the first step (liquid phase process, 490°C, up to 700 bar) a slurry of pulverized coal in a solvent is transformed into a liquid product in the presence of a suspended catalyst and hydrogen. The liquid product boiling below 325°C is converted in the second stage (vapor phase process, 400°C, 300 bar) into light distillates over fixed catalysts in the presence of hydrogen. The solvent required for slurrying the coal is produced in the liquid phase and recycled to the process. About 15 million t of gasoline was produced by the process up to 1945. The plant capacity amounted to about 4 million t/a in 1943 and 1944.

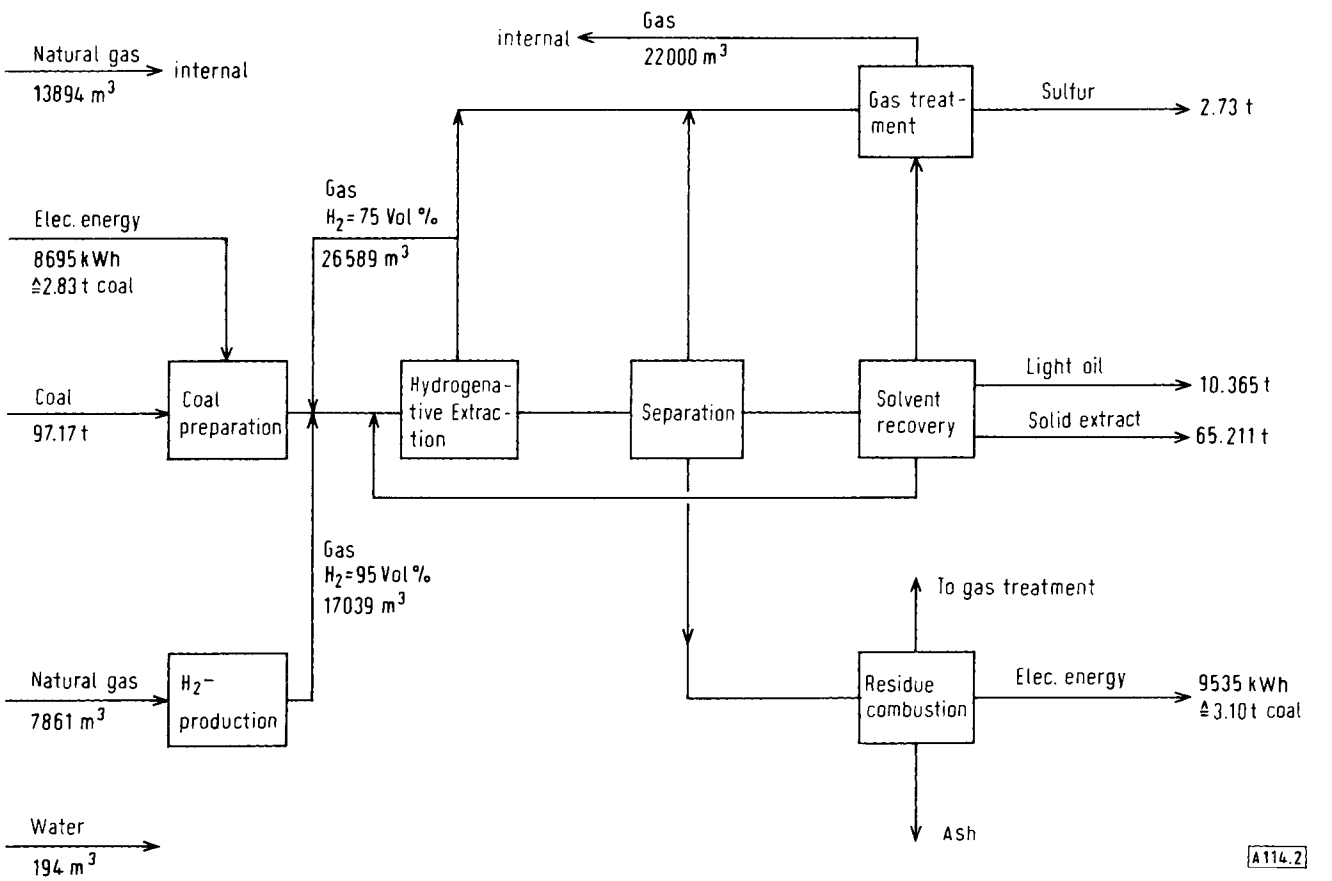

Fig. 2. Block flow diagram of the Gulf SRC-I process.

4.3.4. The Gulf-SRC Process[7]

This process resembles the Uhde-IG process. In the SRC-I process a solid, low-sulfur, low-ash extract is obtained by hydrogenating extraction. Ash and unreacted coal are separated off with the aid of drum filters. The softening point of the extract lies between 160 and 200 °C. Another variant, the SRG-II process, yields liquid products by hydrogenating extraction and destructive hydrogenation. The major product is a low-ash, low-sulfur heavy fuel oil. Production of the solid extract is carried out at 450 °C and 80 bar, and that of the liquid fuel at 450 °C and 140 bar.

Figure 2 shows a block flow diagram of the SRC-I process and its material and heat balance.

The SRC-I process for producing solid extracts has been tested in a 50 t/d pilot plant (Tacoma, Washington, USA). Meanwhile, the plant has been adapted for testing the SRC-II process, which should begin in 1976.

4.3.5. The Consol Synthetic Fuel Process (CSF)[8]

The CSF process of the Consolidated Coal Company was developed on the basis of the Pott-Broche process. It is a two-stage process.

In the first stage the coal is slurried with a solvent arising in the process and extracted at about 400 °C and 20 bar. After removal of ash and unreacted coal, the solid extract is subjected to destructive hydrogenation. A petroleum-like product is obtained.

A pilot plant having a capacity of 18 t/d was operated in Cresap, West Virginia, USA, but was shut down because of difficulties encountered in solids/liquid separation.

4.3.6. The H-Coal Process[9]

In the H-Coal process of Hydrocarbon Research Inc. the coal is converted in a single stage into liquid products in the presence of a cobalt-molybdenum catalyst. The catalyst is retained in the reactor where it is kept in random motion (ebullated bed reactor). Its hydrogenating capacity is maintained by constant removal and replenishment of spent catalyst. Maximum operating temperature and pressure are 460 °C and 200 bar. Depending on the reaction conditions the process can yield predominantly light distillates or fuel oils. A material and heat balance is shown in Figure 3.

The process has so far been tested in a pilot plant consuming 3 t/d of coal. With support from the Energy Research and Development Agency (ERDA) and several US companies, Hydrocarbon Research is currently planning a pilot plant for 600 t/d of coal.

4.3.7. The Clean-Fuel-from-Coal Process (CFFC)

In the Lummus CFFC process coal is subjected to destructive hydrogenation in a single stage with the aid of a cobalt-molybdenum catalyst. The catalyst remains in the reactor, and the process operates at about 440 °C and 200 bar.

Ash and undissolved coal are removed by sedimentation in settling tanks with addition of a flocculating agent (kerosine)[10]. Predominantly light products or fuel oils can be produced.

The process is being tested in a laboratory-scale plant with a coal throughput of 1 t/d.

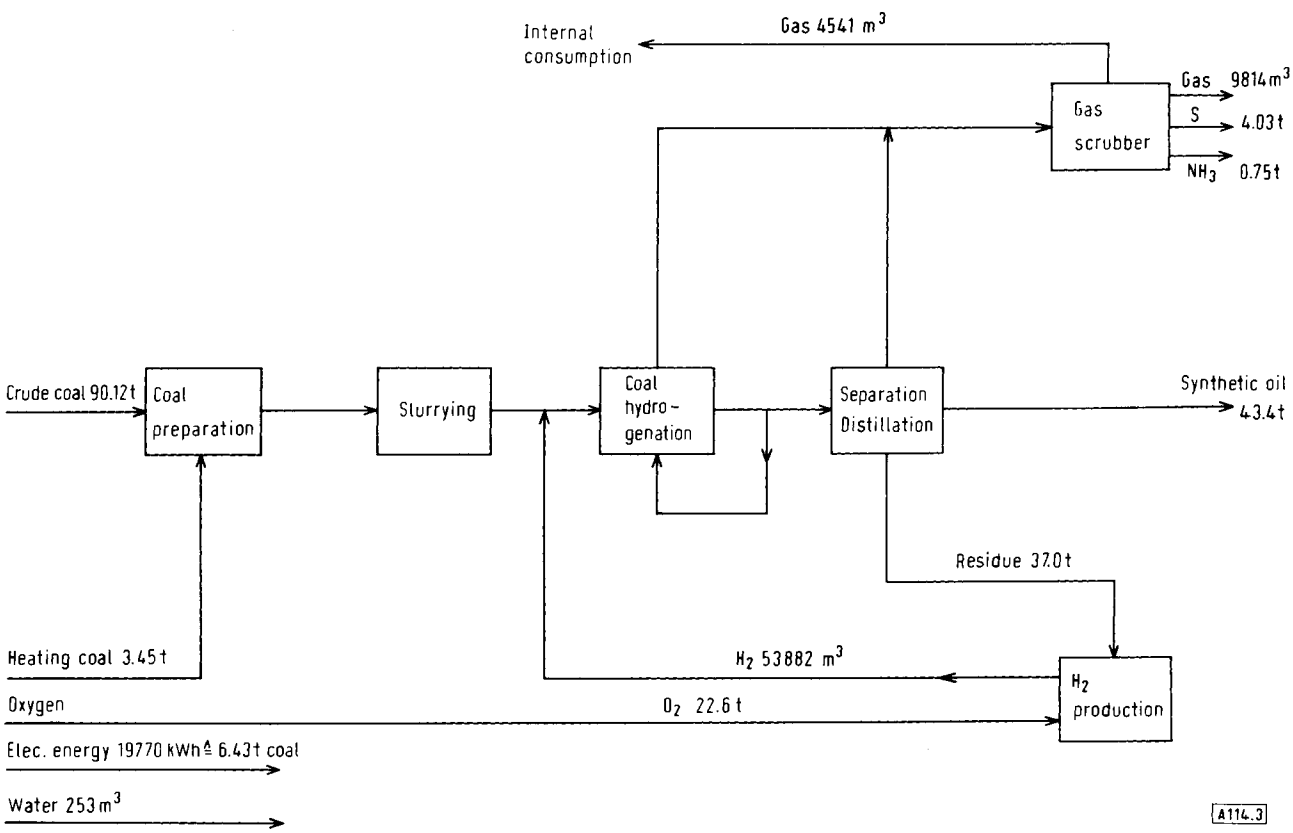

Fig. 3. Block flow diagram of the H-Coal process.

4.3.8. The Synthoil Process[11]

The Bureau of Mines Synthoil process involves destructive hydrogenation of coal slurried with solvent over a fixed bed catalyst at 425 to 450°C and 140 to 280 bar. The process is reported to be suitable for the manufacture of liquid low-sulfur and low-ash fuels for power stations. The technical feasibility of the process has been tested in pilot plant with a coal throughput of 500 kg/d. A pilot plant for a coal throughput of 8 t/d is planned.

4.3.9. The Donor Solvent Process (EDS)

Developed by Exxon, this process yields light distillates to heavy fuel oil. The hydrogen required is provided by the solvent and in the form of molecular hydrogen. The solvent is rehydrogenated catalytically in a second process step. The Exxon company plans to build a pilot plant with a coal throughput of 250 t/d.

4.3.10. Other Activities[12]

Apart from efforts to produce liquid products from coal by extraction or direct hydrogenation, work is also in progress on the conversion of coal into partly liquid products by carbonization. The initially formed low temperature carbonization tar must, however, be hydrotreated prior to further processing. These developments include the COED process (Char Oil Energy Development)[13] of the Food Machinery Company (FMC), the Toscoal process[4] of the Oil Shale Corporation, and the Hydrocarbonization process of the Coalcon Company. The last-mentioned approach utilizes hydrogenating carbonization in order to raise yields of liquid products. A Coalcon pilot plant is being built with the aid of ERDA, the cost being estimated as about 240 million $.

Mention should also be made of a dry hydrogenation of coal at 515°C and 140 bar over a tin chloride catalyst, as developed on a laboratory scale by Utah University[5]. The products are 35% of liquid products (gasoline, Diesel oil), 35% of gas (84% being methane), and 30% of coke. The experiments were carried out batchwise.

5. Technical Problems

5.1. Design Uncertainties

Experience has shown that the design of plant and components for extraction and hydrogenation of coal can be extremely unreliable when based only on analytical data. The consequences are design risks for product quality, functional ability, and capacity. Since the technical basis is uncertain, so are cost predictions. The reason for the uncertainty lies in the fact that the coal from each individual deposit is different. Its influence on the processes of extraction, hydrogenation, and filtration therefore must be experimentally verified.

5.2. Removal of Solids

The removal of solids (mineral components, undissolved coal) from the suspension after extraction or hydrogenation is problematic because the solid particles are very small and the difference in specific gravity between solids and liquid is slight. Furthermore, the adhesion between liquid and solid particles and the viscosity of the liquid are high.

A further obstacle to filtration may be presented by swelling of the primary transformation products of the coal on hydrogenation to form a kind of gel.

Filtration is accomplished mainly with rotary filters, the drums being precoated with a kieselguhr suspension. The layer of solids arising on filtration is continuously peeled from the drum by a doctor knife.

The efficiency and lifetime of the filters have hitherto been unsatisfactory. Filters will have to be developed which permit high-speed filtration and are reliable and easy to operate.

Removal of solids by sedimentation has the advantage of a low energy consumption. However, much space is required. The residence time in the large settling tanks is reduced by addition of flocculating agents. The principal development task consists in determination of the parameters determining the sedimentation process in large-scale plant for the particular kind of coal used. Moreover, the storage stability of the product must also be investigated. There is evidence that asphalts precipitate long after removal of the flocculating agent.

Use of distillation for liquid/solids separation can result in baking and blocking of the distillation column, thus impairing heat transfer. Wear of pumps, fittings, and other plant components by the enriched solids is also to be feared.

5.3. Utilization of Residues

Liquid/solids separation affords a sulfurous residue made up of oil, unreacted coal, and mineral components. Processing of this residue causes problems since dumping or combustion are ruled out by impaired efficiency or environmental pollution. A possible solution lies in heating of the residue to drive off the oil and subsequent gasification of the dry residue, provided that the ash content is not too high. Hydrogen generated on gasification can go some way to cover requirements for hydrogenation.

5.4. Catalyst Behavior

Problems encountered are attrition of the catalyst by the turbulence in the hydrogenation reactor and deactivation by solids deposited on the catalyst surface.

5.5. Performance of Materials of Construction and Plant Components

Plants for manufacture of synthetic liquid fuel from coal operate at temperatures between 450 and 500°C and pressures of 70 to 300 bar. Hydrogen used under these conditions as well as the presence of sulfur and other corrosion-promoting substances place stringent demands on materials. Problems are also raised by the conveying of coal/oil suspensions which can lead to erosion in pipework, fittings, and above all in the highly taxed pumps.

6. Further Developments

Development of a commercially viable process for producing heavy fuel oil and middle and light distillates as feedstock for the chemical industry should be pursued along two lines.

One of the principal paths worth following is the single-stage limited hydrogenation without catalyst. At the present state

of development this kind of process provides an opportunity of achieving the production of low-ash and low-sulfur heavy fuel oil in the fairly near future with relatively simple engineering and on a sound economic basis. Adaptation of the Gulf 50 t/d pilot plant at Tacoma to liquid product will provide the earliest opportunity for large-scale testing of this process variant.

The other main line of development is destructive hydrogenation with the aid of catalysts. This kind of process has greater inherent flexibility (production of heavy fuel oil and of middle and light distillates). It has been tested up to a pilot scale.

The double strategy outlined is necessary in the absence of any clear indication as to which approach offers the greater technical and economic promise. Moreover, it cannot yet be predicted when the processes will reach the goal of commercial viability. Nor can it be ruled out that one of the two approaches will have to be abandoned for technical or economic reasons prior to attainment of that goal.

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Glass—A Continuing Challenge to Chemistry

By Marvin D. Britton[*]

This review of the modern chemistry of glass shows that silicate glasses are extremely reactive materials. Compositions, phases, surfaces, and structures can be manipulated in endless variety, and there is no foreseeable limit to the benefits of research in this area.

1. Introduction

1.1. The Structure of the Glass Industry

In the field of materials science, glass and ceramics are considered to be similar materials, both in respect to their properties and in many of their applications. However, the characteristic which truly distinguishes these materials is the process of forming. Typically, ceramic products are formed by powder compaction, while glass products are manufactured by chilling a completely fused silicate (for general reading, see refs. [1–10]).

This concept of isolating an industry for study on the basis of unique forming concepts can be carried further: the entire glass industry can be split into four major groups, all relying on the melting of mineral raw materials, but each depending on a characteristic forming process and product: the sheet glass industry, the container glass industry, the fiber glass industry, and the technical glass industry. The manufacture of art glass is a fifth branch, but of much less commercial importance. In the United States, containers account for about one-half the dollar volume, technical glass about one-fourth, and glass fibers and flat glass share the balance about equally[11].

1.2. The Economics of the Industry

While almost all elements of the periodic table are used in the glass industry, the oxides of silicon, calcium, and sodium form the "soda-lime glass" which accounts for 95% of the glass produced in the United States. Fortunately, there are no shortages of these raw materials, and given adequate fuel supplies in the future, glass will continue to be one of the most economical materials known to the architect, product engineer, or consumer.

The other 5% of the glasses encompass hundreds of specialty glasses, with several families of compositions developed especially for their optical properties, heat resistance, electrical resistance, ease of fabrication, or durability. Raw materials for such compositions are in generous supply, although economic and political factors have increasingly affected both costs and availability. For example, shortages of soda ash as produced by the Solvay process seriously affected container glass

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production as demand increased, but a 300 year underground supply of trona, a natural deposit, has been opened in Wyoming.

2. Glass Composition and Properties

2.1. The Structure of Glass

Glass should be considered as a state of matter, and is in no sense a unique composition. It is like a liquid in the sense that the composition is infinitely variable and the atomic structure is without long range order. However, there is a difference from a cooling or supercooled liquid: at some point, known as the transformation point, the volume *versus* temperature curve deviates from the straight line that would be followed by a supercooled liquid. The transformation temperature will vary according to the rate at which the liquid is being cooled, and the range of transformation temperatures associated with a particular composition is called the transformation range. The structural changes occurring at the transformation temperature are not known, since there is no definitive knowledge of the cold structure of glass. The difference in behavior from that of a supercooled liquid or a composition which crystallizes on cooling and melts on heating is shown in Figure 1.

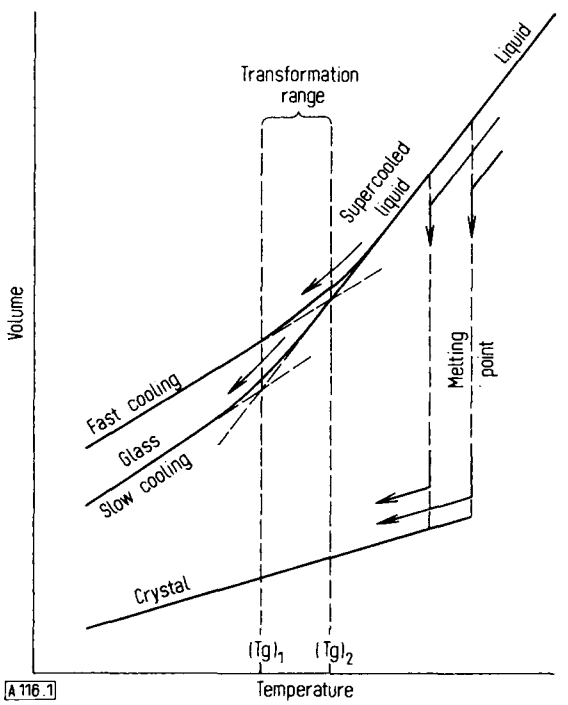


Fig. 1. Volume-temperature relationships for glasses, crystals, and supercooled liquids.

The most common concept of the structure of glass is of a random network of silicon atoms, each surrounded by a tetrahedrally arranged group of four oxygen atoms. This building block, the $[SiO_4]^{4-}$ tetrahedron, shares each of its oxygens with another silicon atom, which is at the center of an adjacent $[SiO_4]^{4-}$ tetrahedron, but the angle of contact between the several tetrahedra is not fixed in a glassy structure. Thus, there is a short range order: the 1.6 Å range of the Si—O couple; but within the distance of 17 Å, there is no longer any semblance of order, the structure being that of the liquid state. The two-dimensional schematic drawing (Fig. 2a) shows the irregularity of structure in contrast with the regular structure of a crystalline silica such as the mineral quartz (Fig. 2b).

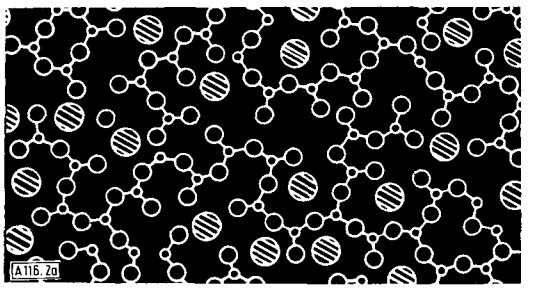


Fig. 2a. Schematic two-dimensional representation of a non-crystalline structure containing network modifying cations.

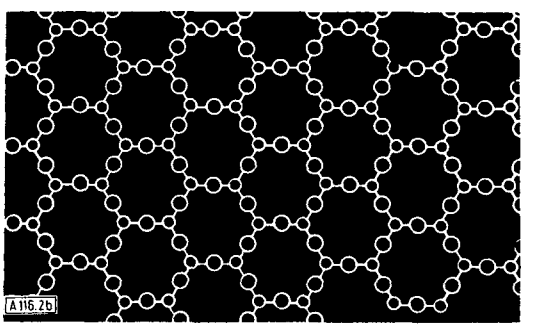


Fig. 2b. Schematic two-dimensional representation of a crystalline silica atomic structure.

Silicon is a network former because of its ability in conjunction with oxygen to maintain a random network on cooling to a solid. B_2O_3 and P_2O_5 behave similarly. The Si—O bond is covalent, and strong enough to make the network rigid even at high temperature. Thus, molten silica is extremely viscous even at 1800 °C, much above the 1713 °C melting point of the original phase, cristabolite. The network forming elements, B, Al, Si, Ge, and others fall in a group for which the E—O single-bond strength ranges from 80 to 120 kcal/mol. The modifying elements, *e.g.*, Mg, Ca, Li, K, Na, Cd, Cs are ionically bonded to oxygens, and this bond strength ranges from 10 to 60 kcal/mol. The network modifiers, being more loosely bonded are relatively free to diffuse through the structure, and this is especially true for the monovalent cations. These modifiers also rupture the continuous Si—O—Si network, and in thus limiting the degree of linkage, substantially reduce the viscosity of the glass at every temperature. Divalent ions act as a bridge between two oxygen ions, and while they break up the strong network structure they are less mobile and less effective fluxes than the univalent cations. The disruptive action of monovalent and divalent cations is illustrated in Figure 2a.

In addition to the network formers and modifiers, a third group, the intermediates, have bond strengths of 60—80 kcal/mol. Typical elements are Ti, Zr, Pb, and Al. Such ions are not usually capable of forming a glass, but can occupy either a glass forming or a glass modifying position, or both.

Relative amounts of the three types of elements can be varied to an almost infinite degree to achieve a particular set of properties. The only constraint is that a sufficient amount of network forming ions must be present to prevent crystallization. These base glasses then serve as a host for the coloring oxides, small quantities being adequate for rich, transparent colors. Examples of these coloring agents are: yellow, UO_2, CdS; green, Cr_2O_3, Fe_2O_3; blue, CoO, FeO; violet, NiO, Mn_2O_3; gray, Cr_3O_4-NiO; black, Mn_2O_3-Cr_2O_3; red, CdSe, colloidal Au or Cu.

2.2. The Homogeneous Glasses

Homogeneous glasses consist of a single phase. They vary widely in composition, but will fall into one of three classes: the "refractory" glasses[12] and the "hard" glasses, meaning that the melting, working, and use temperatures of the glasses are higher than those of the third type, the "soft" glasses. These terms refer to the viscosity-temperature behavior shown in Figure 3 rather than to abrasion resistance.

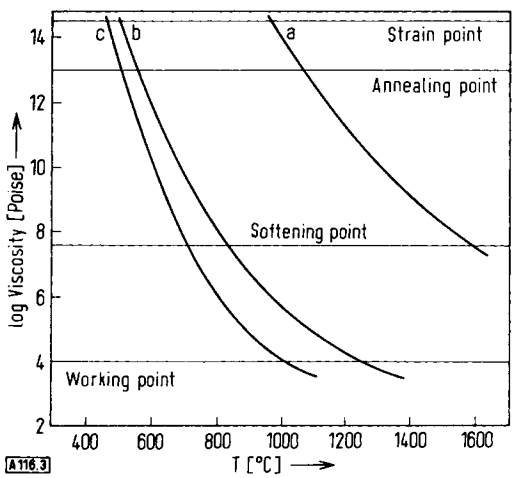


Fig. 3. Viscosity-temperature curves for (a) "refractory", (b) "hard", and (c) "soft" glasses. Compositions: (a) 99.9 % SiO_2; (b) 80.3 % SiO_2, 2.3 % Al_2O_3, 13.3 % B_2O_3, 4.0 % Na_2O; (c) 73.6 % SiO_2, 1.4 % Al_2O_3, 16.2 % Na_2O, 0.4 % K_2O, 3.4 % MgO, 4.8 % CaO, 0.2 % SO_3.

The refractory glasses include two main families: glasses having high silica contents and the aluminate and aluminosilicate glasses. Hard glass comprises the borosilicates. The soft glasses are made up of three families: the soda-lime, the lead, and most of the non-silicate glasses. It should be noted that the glasses are classified by application rather than by strict chemical type since there is no absolute correspondence between a glass composition and its utilization.

The refractory glasses can also be classed as those having an annealing point over 700 °C. This annealing point is defined as that temperature at which the viscosity is about 10^{13} poises, or as that temperature at which the internal stress is substantially relieved within 15 minutes. Thus, a hard glass such as that shown in Figure 3 (b), which is a sodium borosilicate, would not qualify as a refractory glass since its annealing point is 565 °C. An example of a soft glass, a soda-lime glass with an annealing point at 510 °C, is shown in Figure 3 (c). The refractory glasses include vitreous silica, reconstructed glass, high silica, aluminosilicate, and aluminate glasses (see Fig. 3 (a)).

Vitreous silica[13], the most refractory of commercially useful glasses, ranges in annealing point from 1020 to 1200 °C, depending on the raw material and manufacturing method. The significant variable is the OH^- content. If it is below 10 ppm, the annealing point is 1200 °C; but if the OH^- content is increased to 1000 ppm the annealing point drops by 150 °C. At the high temperatures for which vitreous silica is particularly appropriate there is a tendency for the glass to devitrify (crystallize), particularly around 1600 °C, although there is cristobalite growth throughout the temperature range of 1000 to 1723 °C. If Na_2O is present, even as little as ¼ %, the devitrification rate is increased 20- to 30-fold, and the temperature of maximum crystal growth rate drops from 1600 to 1400 °C. Because of its extreme viscosity, vitreous silica is very difficult to melt and to shape as the material tends to be reduced and to volatilize in the forming range.

If 7.5 % (by weight) of TiO_2[14] is added to vitreous silica the expansion coefficient drops from 5.3×10^{-7} cm/cm K to essentially zero. The annealing point remains at 1000 °C, compared to 1084 °C for vitreous silica.

Reconstructed glass of Vycor type is a 96 % SiO_2 material, described in Section 2.3 as a derivative of phase-separated glass. The properties are close to those of vitreous silica, although the decreased number of silicon-oxygen tetrahedra due to the presence of boron-oxygen triangles lowers the annealing temperature. If special efforts are made to reduce the OH^- content, the annealing point is raised, and the infrared transmittance is enhanced. The OH^- absorption band at 2.8 μm tends to reduce the optical transmission of silicate glasses to less than 10 % of the amount of incident light. With a nitriding treatment, *i.e.*, heat treatment of the porous silica residue in ammonia, the final glass will contain trivalent nitrogen in the structure. The annealing point is raised to 1214 °C. Adding 0.1—0.2 % alumina to vitreous silica will also raise the annealing point by as much as 100 °C.

The aluminosilicate glasses (containing, *e.g.*, 57.3 % SiO_2, 15.7 % Al_2O_3, 3.9 % B_2O_3, 0.1 % Na_2O, 6.6 % MgO, 9.4 % CaO, 5.9% BaO, 0.1% As_2O_3)[15], have high annealing points, but can be much more easily produced than the high silica glasses. Because of their relatively low or zero alkali content these glasses will have low expansion, high electrical resistivity, a steep viscosity curve, *i.e.*, a relatively large change in viscosity for a small temperature change, and lower permeability to gases. A principal use of these glasses is as a lower-cost substitute for high-silica glasses in discharge and halogen cycle lamps. Other uses result from the high annealing point: ignition tubes for chemical analyses, aerospace windows, and infrared transmitting applications.

The borosilicate glass family (hard glass type) balances the excellent properties of the vitreous silicas with the ease of manufacture of the soda-lime and lead glasses. Compared to lime or lead glasses, they have markedly superior resistance to chemical attack, a high annealing point, and excellent thermal shock resistance.

The soft glass families, such as the soda-lime, lead, and most of the nonsilicate glasses represent a predominant part of the glass industry. Soda-lime glass, for example, represents 90 % of the tonnage melted owing to its low cost, ease of melting, ease of forming, and excellent durability.

Lead glass is favored for electrical applications because of its high electrical resistivity and easy workability. Premium lead glasses are used for fine crystal ware because of the

high refractive index and for radiation shielding windows because of their radiation absorption.

The nonsilicate glasses contain GeO_2 or sulfur as one of their chief components. Lindemann glass is composed of light atomic weight materials, primarily B_2O_3, and is used as a transmitting medium for X-rays. Rare earth borate glasses have unusually low dispersion at high refractive index and, like phosphate glasses which have both low dispersion and low refractive index, are used for optical instruments. Germanate and arsenic trisulfide glasses are infrared transmitting glasses. The most remarkable property of the chalcogenide glasses is electronic, *i. e.*, these are semiconducting rather than ionically conducting materials. Recent research has shown that the glassy state can be achieved in very unusual systems such as nitrate, acetate, formate, and thiocyanate. Although no useful materials of this kind have yet been discovered, such systems are useful in the research on the structure of glass.

2.3. The Heterogeneous Glasses

Any account of the recent history of glass research must emphasize the importance of phase separation. These new materials, many of which are produced by chemical treatment or by alterations in the distribution of the various chemical species in the glass, can properly be called "heterogeneous glasses". It must be recognized that heterogeneity can exist at various levels: atomic, submicroscopic, microscopic, or even macroscopic. Each of these families will be now be discussed.

The phase separated borosilicate discussed in Section 2.2 is an example of separation on a scale below below the resolution of the optical microscope. It is a liquid-liquid system (Fig. 4).

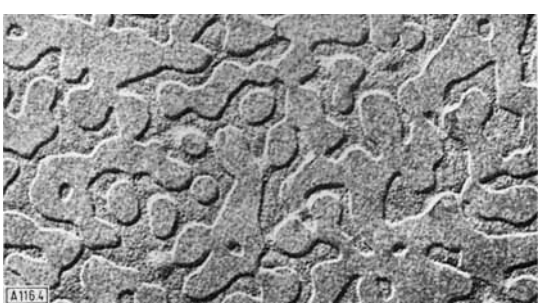


Fig. 4. Electron micrograph of phase separation in a sodium borosilicate glass (composition: see Fig. 3 (b)).

After the mixture has been leached, the residual phase containing 96 % SiO_2 can be reheated to form a condensed structure. In this state the structure is indistinguishable from that of a glass article of the same composition which has been melted and formed in the conventional manner. But there is an earlier stage, the open-structure stage, which is of interest in itself. The porous remains of the leaching process, the so-called "thirsty glass" has an average pore diameter of 40 Å, a surface area of 2×10^6 cm^2/g, a total pore volume of 35 %, and a water absorption of 25 %. The porosity is continuous, and the flow constant of water is 0.00065 ml/cm^2 atm h. While this ultra-fine filter has been experimentally useful in physical and chemical research, newer materials having larger pores have been developed (see Section 2.4). Pore diameters, increased by heat treatment followed by leaching the skeletal structure with mild NaOH or Na_2CO_3 solutions, can reach 2000 Å.

On reheating the 96 % SiO_2-glass skeleton, a shrinkage of 35 % in volume or about 14 % in linear dimension occurs. The properties of such a glass are comparable to those of a fused silica, and more refractory than those of the commercial heat-resistant glass (Table 1).

Table 1. Properties of some glasses.

Glass type	Thermal expansion (0—300 °C) cm/cm K	Softening point [°C]	Annealing point [°C]
Reconstructed [a]	7.5×10^{-7}	1530	1020
Borosilicate (see Fig. 3 (b))	32.5	821	560
Fused silica (see Fig. 3 (a))	5.5	1580	1084

[a] Composition: 96.6 % SiO_2, 0.3 % Al_2O_3, 3.0 % B_2O_3.

Because the glassy state is not a thermodynamically stable phase below the liquidus temperature, it is not surprising that separation of solid phases occurs. What is surprising is the diversity of the phases, the diversity of the mechanics of separation and the complexity of the separation processes. These processes may be studied because of the overriding effect of the high viscosity of glass on the reaction kinetics. That is, high temperature equilibrium states can be "frozen" by cooling the glass to a rigid state, so that expected reactions never occur, or occur at will by controlling the thermal history of the glass.

The first examples of crystal-separation in glass date back hundreds of years[16]. One type, the opal glasses, results simply from exsolution of crystals when the glass temperature drops below the liquidus temperature. Usually fluorides or phosphates of sodium and calcium are precipitated. The second type, gold or copper ruby glasses result from a far more complex reaction; these glasses are initially clear and colorless, and the color appears only after reheating, when colloidal precipitates of the metal are formed.

These processes are very sensitive to oxidation-reduction reactions involving copper in its various valence states. Multivalent ions such as tin, selenium, arsenic, and antimony act as reducing agents for Cu^+ at low temperatures. Cu^+ is generated by melting the glass in a controlled neutral atmosphere; on reheating below 1400 °C, at the lowest temperature at which diffusion can take place, the copper is reduced to the insoluble metal:

$$2\,Cu^+ + Sn^{2+} \rightarrow 2\,Cu + Sn^{4+}$$

If the concentration of reducing agent is decreased, the Cu^+ can absorb ultraviolet light at room temperature and disproportionate on reheating:

$$2\,Cu^+ + h\nu \rightarrow Cu + Cu^{2+}$$

In this photosensitive process a latent image consisting of photoelectrons trapped at Cu^+ ions is formed at room temperature, and the reaction is completed on reheating. With dissolved colorless gold ions, a sensitizer is needed to absorb ultraviolet light and thereby transfer electrons to reduce the gold ions to gold atoms. Cerium oxide is such a sensitizer; Ce^{3+} provides electrons which are trapped in the rigid glass.

While the photosensitive glasses are not commercially important, the concept of photosensitively precipitating metal crystals to act as nuclei for the subsequent crystallization of oxide or silicate phases is of great technical significance. The first development of this type was with lithium metasilicate crystals growing on nuclei of copper, silver, or gold. To act as a nucleus for lithium silicate, the silver or gold particle must have a minimum diameter of 80 Å. Barium disilicate is another separable phase. Sodium fluoride opalescent glasses will similarly separate if subjected to double heating, with a cooling cycle in between. Because the silicate crystals are more soluble in mineral acids than the surrounding glass regions, complex patterns can be developed photographically, then chemically etched into or even through the glass. These chemically machinable, intricately conformed materials have become commercially important. Figure 5 shows the parts for a fluidic control block. The upper sheet illustrates the crystallized portions of the glass; the lower sheet illustrates the residual material after the etching process has removed the crystalline portions of the material.

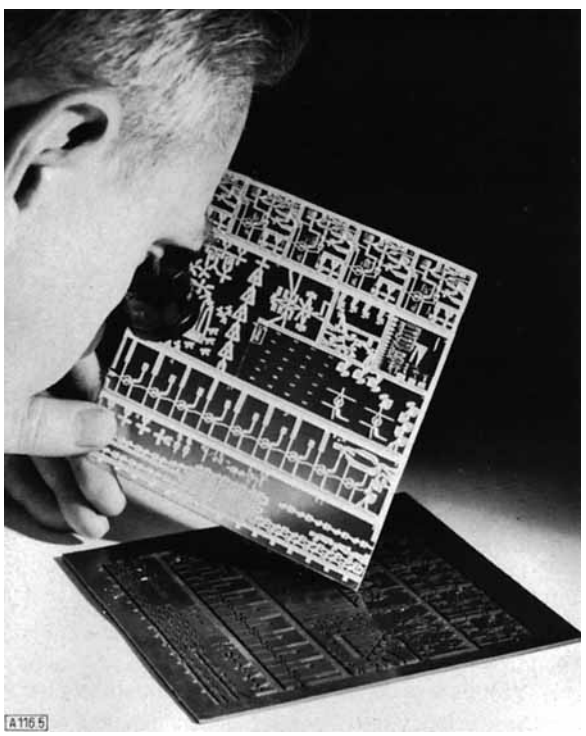


Fig. 5. Intricate glass products produced by photoinduced phase separation and subsequent selective etching (see text).

The concept of photosensitized nucleation and subsequent separation of silicate minerals can be more generally applied to a totally heat-sensitive process. This field of glass-ceramics[17] has developed into many applications, and research programs to discover new materials are being pursued all over the world. A number of substances are known to separate readily in colloidal-size particles in glass: fluorides, phosphates, TiO_2, ZrO_2, and others. TiO_2 is almost universally used as nucleating agent, being especially effective in MgO-Al_2O_3-SiO_2 and Li_2O-Al_2O_3-SiO_2 glasses. These are chemically complex systems, as shown in Scheme 1.

In the various glass ceramic systems it can be generalized that precipitation of β-spodumene, cordierite, and quartz solid solutions produces ultralow thermal expansion behavior; mullite and celsian produce more refractory materials, and mica produces a ceramic capable of being machined using steel tools. The advantages of such materials, characterized by a structure consisting of fine-grained, randomly oriented crystals with some residual glass, but no voids, microcracks, or other porosity, are:

Stage 1 Cordierite glass: $2\,MgO \cdot 2\,Al_2O_3 \cdot 5\,SiO_2$ + TiO_2 catalyst

↓ Δ, 700 °C

Stage 2 Emulsion: colloidal droplets of low-SiO_2 glass in matrix of high-SiO_2 glass

↙ Low silica glass droplets ↘ High-SiO_2 glass matrix

↓ Δ, 800 °C

Stage 3 $MgTiO_3$ crystal nuclei and glass

↓ Δ, 900 °C

Stage 4 Quartz solid solution crystallites

↓ Δ, 1200 °C ↓ Δ, 1200 °C

Stage 5 Cordierite + TiO_2 crystallites Cristobalite

Scheme 1. Processes occurring on heating of a cordierite glass.

1) Flexibility and ease of forming, since all the normal glass-forming techniques can be used.

2) Feasibility of inspecting the transparent glass article for defects prior to crystallization.

3) Uniformity and reproducibility of properties in extremely fine-grained crystalline materials, *i.e.*, uniform thermal expansion.

4) Lack of porosity.

5) Feasibility of strengthening by chemical exchanges.

6) Economy of high volume manufacturing associated with conventional glass manufacturing operations.

If a molten silicate is cooled to a point that immiscible liquids form on a microscopic scale, the stage is set for further crystallization. This nucleation process is easily observed in the Al_2O_3-SiO_2 system in the composition range from silica to mullite ($3Al_2O_3 \cdot 2SiO_2$). The alumina-rich glass readily crystallizes upon heating the emulsion, but the siliceous glass ultimately crystallizes to cristobalite. Structural incompatibility is probably the reason for the separation into two liquids. At high temperature the liquid is composed of partially linked $[SiO_4]^{4-}$ and $[AlO_4]^{4-}$ tetrahedra. On cooling, the melt polymerizes towards a corner-shared tetrahedral array, requiring the coupling of an oxygen to three rather than the normal two tetrahedra. Apparently there is only limited tolerance for this array.

More complex aluminosilicate glasses avoid this anomaly because the interstitially placed alkali and alkaline earth ions provide a charge balance for the trivalent aluminum and normal coupling between tetrahedra is achieved at all temperatures. Thus, addition of another ion, such as titanium, which neither modifies the structure nor supplants the silicon in the structure, is necessary. Less than 10 mol% of TiO_2 induces separation of another glass phase. When the glass is reheated, titanates form from the TiO_2-rich phase, and then act as effective heterogeneous nuclei for the subsequent crystallization of the major aluminosilicate components. In the aluminosilicate glasses of commercial importance the nucleating agents are listed in Table 2.

The amorphous phase separates into particles less than 1000 Å in diameter, producing an enormous surface area on which the primary crystalline nuclei can form. Because the

Table 2. Nucleating agents for aluminosilicate glasses.

System	Nucleating agent	Primary crystalline nuclei	
SiO_2-Al_2O_3-Li_2O	TiO_2	$Al_2Ti_2O_7$	(metastable)
SiO_2-Al_2O_3-Li_2O	ZrO_2	ZrO_2	(metastable)
SiO_2-Al_2O_3-Li_2O	Ta_2O_5	$LiTaO_3$	
SiO_2-Al_2O_3-MgO	ZrO_2	ZrO_2	(metastable)
SiO_2-Al_2O_3-MgO	WO_3	$MgWO_4$	

major crystals also have a small particle size, local stresses due to differences in thermal expansion between phases, anisotropic expansion of crystals, and densification during crystallization are minimized. A major part of the crystallization occurs at viscosities of 10^{10} to 10^{14} poises, just above the annealing temperature, and distortion of the glass during crystallization is minimized.

The newest family of glass ceramics is based on the crystallization of mica-like sheet silicate structures[18]. The fluorine aluminosilicates (mica) have excellent cleavage because of weak crossbonding between the sheets. Fracture propagation across the sheets is very difficult so that fractures follow crystal boundaries. Individual crystals or small groups of crystals and enclosed glass regions thus break apart by pulverizing. These materials are machinable with metal tools and show less sensitivity to surface damage and greater resistance to brittle fracture than do most ceramics.

Now, glass ceramics containing more than two-thirds of mica by volume are normally machinable regardless of the morphology of the mica crystals, but if the mica component is as little as one-half of the volume, the material can be machined only if the aspect ratio of the crystals is high enough

Fig. 6a. Low aspect ratio phlogopite crystals.

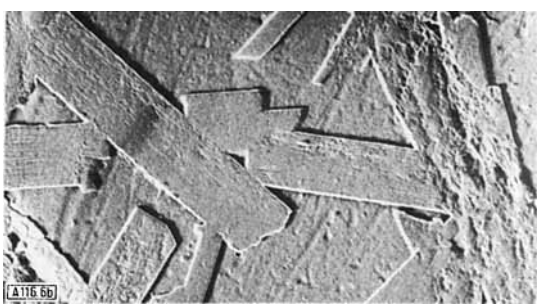


Fig. 6b. High aspect ratio interlocking crystals (flaky structure producing better machinability and thermal shock resistance).

to cause general contact on interlocking of the crystals. The two different microstructures typical of the glass ceramics with synthetic mica are shown in Figure 6a and 6b.

The aspect (diameter : thickness) ratio of the individual crystal can vary from two (thick books; Fig. 6a) to over ten (flakey sheets; Fig. 6b), and during the crystal growth stage depends on the cross-bonding in the crystal and the viscosity of the host glass. Weakly crossbonded micas grow more nearly two dimensionally. Crystals grown in a viscous host are more block-like in form simply due to the difficulties attending diffusion of the necessary ions over long distances.

These materials are composed of K_2O, MgO, Al_2O_3, B_2O_3, SiO_2, and F. They are melted at about 1450 °C, and are crystallized to 50—75 volume percent fluorophlogopite crystals by heating at 950—1050 °C for 2—4 hours. The nucleation step always necessary before crystallizing the glass ceramics occurs on cooling the glass without quenching or thermal soaking. Immiscible liquids are formed because Mg^{2+} ions combine with Al_2O_3, B_2O_3, and K_2O to form a low-SiO_2 matrix glass. Apparently the Mg^{2+} ions shift from a coordination number of 4 to a coordination number of 6. This is analogous to the 4 to 6 shift in the coordination number of titanium, a common nucleating ion for other glass ceramics. The process of crystallization is not a simple process, however. It involves the heterogeneous nucleation of chondrodite crystals and their dendritic growth in the matrix glass, followed by recrystallization of the chondrodite to norbergite, and subsequent grain growth of the phlogopite crystals into a highly interlocked microstructure.

While the glass ceramics are usually opaque, transparent varieties have also been discovered[19]. Either the crystallites of all species must be much smaller than the wavelength of visible light or the birefringence within the crystals and the refractive index difference between crystals and the host glass must be very small. These conditions are satisfied in several aluminosilicate systems containing β-quartz solid solutions, spinel, or mullite as the major crystalline phases. The β-quartz family produces materials that are refractory, of ultra-low expansion, and of high electrical resistivity. All members of the family have high thermal shock resistance, chemical durability, and crystallinity. The spinel and mullite glass-ceramic families contain considerable host glass, but still have excellent transparency, even after exposure to temperatures above 1000 °C for long periods. Such fine-grained materials are able to take an optical polish, permitting their use in reflective optic applications where the special property of an extremely low thermal expansion is desired.

Another aspect of nucleation and crystallization from glasses is demonstrated by the special family of photochromic glasses[20, 21]. Silver halide, the photosensitive phase, is precipitated from the host glass. Such materials, which darken when exposed to ultraviolet light and lighten when the ultraviolet is removed, do not seem to ever loose this capability, have high resolution capability, high darkening sensitivity, and a wide range of fading rates. Thus, special glasses can be designed for many applications because the physical properties are independent of optical properties, and optical bleaching (reversion) is independent of thermal bleaching.

The base glass of the most intensely studied photochromic system is an alkali boroaluminosilicate. Silver and halogen ions are dissolved in the glass and the halide crystallites are developed by holding the homogeneous glass at temperatures

between 500 and 700 °C for periods of 15 minutes to 4 hours. The most useful crystallite size is between 50 and 200 Å. If the crystals are smaller, the glass darkens poorly; if larger, the glass is hazy. The average spacing between particles is about 1000 Å.

A small amount of copper increases the darkening sensitivity by a factor of 100 or more, and the choice of halogen strongly affects the photochromic properties: as the atomic number of the halogen increases the fundamental absorption edge of the silver halide shifts to longer wavelength; thus the darkening sensitivity is extended. Furthermore, the solubilities of the various silver halides differ considerably in most base glasses. Obviously, the base glass composition, *i.e.*, the amount of lead, alkali, and boric oxide, affects the physical properties of the glass, but a most important function of the host glass composition is the temperature dependence of the silver halide solubility. In a good host glass, the solubility of the silver halide is high at the high temperature used to melt the glass, but low at intermediate temperature. Thus, the glass can be supersaturated with the halide and the excess solute can be precipitated out by heating at an intermediate temperature.

Heat treatment dictates the photochromic properties as much as composition, *e.g.*, the number and size of particles can be independently controlled by adjusting the nucleation and growth times. The fade rate constant decreases with increasing particle size, but particles less than a critical size will not darken.

The ultraviolet absorption is independent of particle size, and the darkening achieved is affected by the penetration of the light. Thus, while darkening and fading rates depend on the particle size distribution because the darkening and fading constants depend on particle size, the ultraviolet absorption depends on the total amount of silver halide precipitated. Furthermore, the photochromic absorption spectrum changes shape with the particle size: small particles make a glass appear pink while large particles make a glass appear blue-gray.

Composite structures of glass exist at all levels: macroscopic, microscopic, submicroscopic, and atomic. The complex array of lenses used in most cameras is made of different lens elements, each of which is a different composition and has different properties; at the microscopic level, a glaze on a porcelain or china dish will be of different composition and properties than the base material. At the submicroscopic level, liquid-liquid phase separation results in immiscible glasses which differ in composition and properties, and can be clearly recognized if one phase is etched and the material examined by the electron microscope. At the atomic level, glass is a composite in that it is composed of many different ions, but if the melt is well mixed, it is essentially homogeneous. This last condition can be altered to produce atomically composite structures of great utility. This process includes alteration either after forming or before forming the finished article.

There are two types of treatment applied after the glass article is formed: composition alteration at the surface by ion-exchange and phase alteration of the surface by crystallization. The first process results in surface compression or tension due to differential thermal expansion. For example, once lithium ions from a molten salt bath (*e.g.* lithium and sodium sulfate) are exchanged for sodium ions in the host glass at a temperature above the annealing point of the glass, the thermal expansion of the skin will be less than that of the core. On cooling, the shrinking of the higher expansion core will pull the skin into compression.

Ion exchange can also involve exchanging large ions, such as K^+ in the bath for smaller ions such as Na^+ in the glass. The skin, being expanded at the higher temperature will be stuffed, and will not shrink as much as the core. Again, the compressed surface greatly strengthens the glass. This process is done below the annealing point of the host glass, and thus the effect results from the inability of the glass to relieve the induced strain. The "stuffing" process is applicable to the replacement of Li^+ ions in the glass by Na^+ from a molten salt bath, but is less commonly used because of the high cost of lithium materials. Thus, the most satisfactory base glass is within the soda-alumina-silica system. The change in composition can be detected by an electron microprobe (Fig. 7).

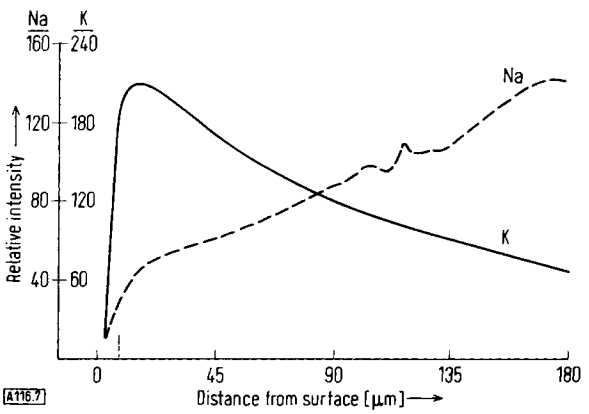


Fig. 7. Relative alkali ion concentration change of surface of sodium glass after immersion in a potassium salt bath.

While this stuffing is done at a temperature below the transformation range of the glass, long exposure to temperatures above 200 °C can result in substantial loss of strength because of ion migration. As was done with the case of multi-pane windows for the space capsules, such chemically strengthened glasses can be protected from transient high temperature by other panes of heat resistant, lower strength, refractory glasses.

Although the cost of the lithia-based glasses is more than that of the soda glasses, the more important difference is in their rates of ion exchange. At 400 °C, the Na^+ for Li^+ exchange rate using a $NaNO_3$ melt is ten times that of the K^+ for Na^+ exchange. To get adequate depth of penetration to produce an abrasion resistant skin the soda-alumina-silica glass must be treated in potassium nitrate at temperatures 100 to 150° higher than for the lithia-alumina-silica glass. The chemical durability of ion-exchanged glasses is better than that of the base glass, suggesting that leachability is a function of the stress level.

Surface strengthening is achieved by crystallization at the surface of materials having particular compositions, *e.g.*, 67 % SiO_2, 26 % Al_2O_3, and 5 % Li_2O with minor constituents: 0.1 % K_2O, 0.3 % Na_2O, 0.1 % B_2O_3, 0.8 % TiO_2, and 0.5 % As_2O_3. Some surface-crystallized specimens of compositions in the Li_2O-Al_2O_3-SiO_2 system achieved a modulus of rupture strength of over 70 kg/mm^2, compared to an uncrystallized glass strength of the order of 3 kg/mm^2. This finding can be rationalized as follows: in order for a quartz-like phase to precipitate, one Li^+ ion is needed for each Al^{3+} ion. Since

the glass is deficient in Li^+ ions, crystallization of the surface layer drains the adjacent interior region of Li^+ ions. Because the relative growth rate is proportional to the concentration of the Li^+ ions, the process ultimately becomes diffusion controlled.

The phenomenon common to all present-day modes of glass strengthening is surface compression. With the exception of thermal tempering, alteration is accomplished by a change in glass composition at the surface relative to the core. Production of laminates has been practiced for artistic purposes for many years, but Schott was probably the first to do this for technical purposes. The modern technique, unlike Schott's process of overlaying one gather of glass with another, is to simultaneously draw three ribbons, thus forming a sheet with two similar skins and a dissimilar core. The relative physical properties of such glass pairs are extremely important: the rheological properties for drawing the sheet and the expansion properties for establishing the ability of the laminate to remain bonded and yet achieve a high level of strength. Of most interest to the chemist is the nature of ion diffusion at the skin-core interface[22]. Diffusion distances for sodium and other ions can be readily estimated with the electron microprobe and are found to be substantial. For commercial laminates diffusion distances from less than 8 to as much as 30 μm have been found, and diffusion is, as would be expected, greater in the glass with the lower softening point.

Much has been written about the startling performance of optical waveguides for telephone systems, data transmission, and instrumentation. The usual cable has six step-index doped deposited silica optical waveguides with a maximum attenuation of 20 dB/km at the 820 nm wavelength. The individual fibers in a cable have an outside diameter of of 135 μm, and a core diameter of 85 μm. The fused silica family of glasses was chosen because of low intrinsic scattering and absorption loss and this functionally complex glass fiber is produced by an exacting chemical process to produce a material of extraordinary purity. Because of optical absorptivity, transition element contamination could not be tolerated beyond a few hundred parts per billion, thus the final choise of process involved vapor phase reaction using high purity vapors distilled from liquid starting materials. From this vapor, a highly reactive soot was condensed onto a mandrel to provide glass blanks for redrawing into a fiber. To raise the refractive index at the appropriate position in the glass blank, GeO_2 is added, again as a vapor phase addition. TiO_2 also had a favorable influence on refractive index and expansion, but at the high temperature required, the oxide was reduced and absorption losses increased.

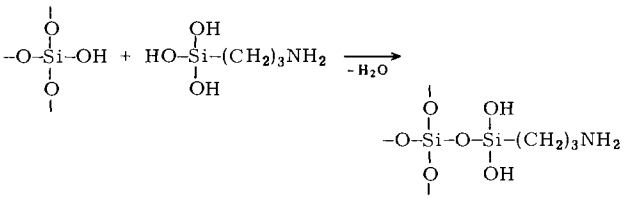
2.4. Surface-Active Glasses

Its use as a vessel for the storage of thousands of different liquids deludes us into thinking of glass as being chemically inert. This, while practically correct, is far from the truth, of course, and resistance to chemical attack on glass is an essential criterion for performance. Less well known is the surface activity of glass, and both organic and inorganic species can be chemically bonded.

Organic molecules are bound to glass by silane coupling. In the presence of water, a monomeric alkoxysilane having an organofunctional group will hydrolyze thus:

$$H_2N(CH_2)_3\text{-}Si(OC_2H_5)_3 \xrightarrow[-C_2H_5OH]{+H_2O} H_2N(CH_2)_3\text{-}Si(OH)_3$$

The hydrolyzed silane then reacts with the OH group on the glass surface to form an aminoalkyl-glass composite:



The activated glass surface can be reacted in standard organic fashion to directly couple biological molecules. Proteins[23] are readily coupled, *e.g.*, the enzymes commonly used to catalyze reactions in food processing. The advantage of fixing such agents is that on-line processes can supplant batch processes, with significant improvement in efficiency and in the useful life of the enzyme. Starch can be converted to glucose, whey can be converted to a useful milk solid. In one application, solid phase radioimmunoassay, controlled pore size glass is used as a substrate carrier. Antibodies are immobilized by silanization of the glass, using a glass particle of about 1 μm diameter and a pore surface of as much as 200 m^2/g. It is expected that this new branch of glass chemistry will find many applications in the field of food processing, medicine, chemical analysis, and pharmacy.

Inorganic species of most recent interest include iron oxide films and chromium films for photofabrication masks. The chromium masks are quite familiar, being a technology that with some refinement was put directly into use when the masking requirements arose in the late 1960's. Iron oxide masks[24] are manufactured by a similar process, *i.e.* high energy reactive sputtering, and at about the same cost. They have lower defect densities, and should supplant the chromium masks. The function of the glass is much more than simply a low expansion, transparent material. It can mean greater durability, increased scratch resistance, better ultraviolet transmission, improved flatness, reduced contamination from chipping of mask edges, and better pattern definition. The type of glass chosen plays an important role in mask performance. While durability is not a key point, scratch hardness is. Films on borosilicate glass are about $2\frac{1}{2}$ times more scratch resistant than those on a soda-lime glass.

The surface chemistry of glass is complex and depends on several factors, *e.g.* the initial pH of the corroding solution, the changes in pH which occur as the glass is leached, a film on the glass, or a film deposited as a reaction interface, ion exchange between the glass and the corroding solution, and phase separation within the glass which leads to nonuniform attack. As for the fundamental mechanism of attack, glass is not dissolved by water but is hydrolytically decomposed. Hydrolysis occurs preferentially at the Si—O—M (alkali or alkaline earth) bond rather than the Si—O—Si bond. The original Si—O—M element of structure is thus converted into Si—O—H and a hydroxide of M. A surface gel forms which contains both the original Si—O—M elements and the newly formed Si—OH elements. Penetration of the proton further into the glass structure is a diffusion process, but if the increasing quantity of alkaline hydrolysis products is not removed, a kind of alkaline attack will then occur and nullify the hydrolytic process. Below pH 7, alkali or

alkaline earth ions are replaced by H^+, but the Si—O—Si element of structure is unaffected. Alkali solutions will break the Si—O—Si elements to form both Si—O—M and Si—OH groups. Alkali attack then progresses linearly with time, and is more intensive than either water or acid attack[25].

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Eutrophication and Wastewater Purification

By Dietrich Gleisberg, Joachim Kandler, Hansjörg Ulrich, and Peter Hartz[*]

One of the nuisance conditions brought about by the impact of civilization on some regions is the accelerated eutrophication of receiving waters, especially of stagnant waters, owing to the increased supply of plant nutrients from industrial and municipal wastes. To counteract this situation it is recommended that effective measures be taken to reduce the supply of phosphorus and, in part, nitrogen to such waters. Insofar as the supply of these elements stems from communal wastewaters this objective can be achieved by extensive purification. While the most suitable method for removal of nitrogen is nitrification and denitrification, that which recommends itself for the removal of phosphorus is the method of phosphate precipitation, a well established, economic technique which can be employed in existing plant. The success of the measures taken, however, depends to a large extent on achieving wastewater having a very low phosphorus content.

1. Causes and Effects of Eutrophication

1.1. Eutrophication Phenomena

By eutrophication is understood the enrichment of nutrients in surface waters. It also embraces the phenomena which are observed as a result of nutrient enrichment, particularly in stagnant and slowly running waters[1]. Eutrophication is a natural aging process, which, however, can be accelerated and altered by communal influences. The copious supply of nutrients leads primarily to increased growth of aquatic plants, especially of plankton algae. It can lead to extensive propagation of algae, to "lake blooms", having an unusually high algae density (number of algae per unit volume).

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In addition to the favorable increase in production of animal plankton and fishes, however, the overall consequence of such an algal growth is a negative one. The algae sink, especially on dying, from the upper layers of the water to the growth zone in deeper layers, where they undergo bacterial decomposition; a process involving consumption of large amounts of oxygen. The resulting decrease in oxygen content in the deeper layers is typical of eutrophic lakes[2]. The withdrawal of drinking water can become problematical, and fish spawn can suffer asphyxiation. Finally, anaerobic chemical transformations, with liberation of *e.g.* hydrogen sulfide, can take place on the bed of such a water. The deficiency of oxygen in the water can be replenished only after the summer stagnation when the water is driven into circulation by the wind during the fall and spring time.

A further characteristic of eutrophication is a change in the type and variety of algae. During the transformation of a lake from the oligotrophic, *i.e.* less nourished state, into the eutrophic state, diatomaceae are displaced by green algae,

and these in turn by blue-green algae, whereupon the number of incident types frequently decreases[3].

1.2. Geographical Location

The transformation of oligotrophic, *i.e.* nutrient-deficient water into the eutrophic state has in recent years been mainly observed in those regions where civilization has had a noticeable influence on environmental conditions in the neighborhood of stationary waters, *i.e.* in North America, Scandinavia, and the Netherlands, as well as in the Federal Republic of Germany in Schleswig-Holstein, South Germany, and in some artificial reservoirs. In the Federal Republic of Germany some 5% of the population live in the catchment area of such a water[4].

Eutrophication phenomena are far less discernable in flowing waters than in stagnant waters. The reasons for this are, *inter alia*, that nutrients can be more highly enriched in stagnant waters, since those already taken up by aquatic plants are partly available again after the plants have decayed. Moreover the upper layers of stagnant waters become warmer owing to far less turbulence, and the fact that passage of light is not so impaired by suspended material as in flowing waters[5]. The limiting velocity of flow below which the most intense algal growth is favored has been quoted as 0.3 m/s[6].

Eutrophication is not fundamentally limited to fresh water; it even extends to coastal water[7], creeks, bay[8], and the open sea[9]. In each case, however, the phenomena observed can be rationalized in terms of local conditions.

1.3. Causes of Eutrophication

1.3.1. Algal Growth

The primary production and growth of flora in waters depends on several parameters, including, light, temperature, and water motion[1]. The enhanced growth of such flora resulting from the impact of civilization is due, however, to the increased supply of nutrients that are as necessary for aquatic plants as they are for terrestial plants. Analysis of the dry matter obtained from a few types of algae occurring in eutrophic lakes gives an indication of the most important nutritional elements (Table 1)[10].

Table 1. Composition of dry solids from blue-green algae and green algae [10].

Element [%]	Blue-green alge *Microcystis*	Blue-green algae *Anabaena*	Green algae *Cladophora*
C	46.5	49.7	35.3
N	8.1	9.4	2.3
P	0.7	0.77	0.56
K	0.8	1.2	6.1
Ca	0.53	0.36	1.7
S	0.27	0.53	1.6
Fe	0.27	0.08	0.23
Mg	0.17	0.42	0.23
Na	0.04	0.18	0.18
Mn	0.03	0.008	0.10
Zn	0.005	0.000	0.001
Cu	0.004	0.007	0.019
B	0.0004	—	0.0085

In addition to the elements quoted in Table 1, several others, including molybdenum, vanadium, chlorine, cobalt, silicon were also found to be present—in some cases as many as 20 elements were detected[11]. All of these essential nutrients are contained in the "New Algal Assay Medium" (NAAM), the nutrient solution proposed for laboratory testing of the degree of eutrophication of waters (Table 2)[12].

Table 2. Composition of the nutrient solution NAAM (New Algal Assay Medium) [12].

	[mg/l]		[μg/l]
$NaNO_3$	25.5	H_3BO_3	185.64
K_2HPO_4	1.044	$MnCl_2$	265.27
$MgCl_2 \cdot 6H_2O$	12.39	$ZnCl_2$	32.7
$MgSO_4 \cdot 7H_2O$	14.7	$CoCl_2$	0.78
$CaCl_2 \cdot 2H_2O$	4.41	$CuCl_2$	0.009
$NaHCO_3$	15.0	$Na_2MoO_4 \cdot 2H_2O$	7.26
$Na_2SiO_3 \cdot 5H_2O$	92.7	$FeCl_3$	96.00
		$Na_2EDTA \cdot 2H_2O$	300.000

Of the most essential nutrients, carbon is generally available in abundance, since the carbon dioxide dissolved in the water and the CO_3^{2-} ions and HCO_3^- ions that are in equilibrium with it are supplemented by that from the atmosphere and that arising from the bacterial degradation of organic substances[13]. In most waters nitrogen is available in excess, like potassium and calcium as well as sulfur and iron, since bacteria and blue-green algae are capable of fixing atmospheric nitrogen in organic compounds.

1.3.2. Limitation of Algal Growth

In investigations on the growth limitation factor, the minimum factor as defined by the Liebig law[14], a variety of results had to be obtained for each of the large number of influences relevant to algal growth. Thus, in numerous cases phosphorus was determined as growth limiting[15–18], in other cases the elements nitrogen, iron, carbon, cobalt, magnesium, molybdenum, zinc and magnanese[19–27].

Nevertheless, in order to develop a universally applicable strategy for combatting eutrophication, the view taken presently is that less importance attaches to the question of which substance be under consideration as the minimum factor in an actual case than to whether an element (or possibly two elements) can be effectively restrained from entering the receiving waters. If it is possible to bring the content of this element in the water down to a very low level then it can generally take over the key role of the minimum factor. In this sense efforts have concentrated on phosphorus, and with certain reservations on nitrogen, as the elements which are the main contributors to the eutrophication of receiving waters as a result of the impact of civilization.

Sawyer[28] has quoted a value of 0.01 mg P/l as the most likely concentration below which phosphorus can be expected to have little influence. Other authors quote higher values. An exact determination is complicated by the fact that many algae are capable of storing up to 30 times more phosphorus than they actually require and then releasing it again[3]. More informative as a limiting value, which can only apply for the period after full circulation in the spring, might be the permissible surface loading of a lake. According to *Vollenweider* this amounts to 0.2—0.5 g total-P and 5—10 g total-N per m^2 and year for oligotrophic lakes. Lakes with a yearly loading of *e.g.* 1 g total-P/m^2 and simultaneously 10 g total-N/m^2

are eutrophic. The depth of the lake is an additional parameter which must be taken into account[29].

1.3.3. Nutrient Sources

A systematic overview of all possible sources of phosphorus has been compiled by *Coughlin*[30] (Table 3).

Table 3. Sources of phosphorus [30].

1. Localizable origin
   - 1.1. Effluents from built up areas and municipalities
     - 1.1.1. Human excrements
     - 1.1.2. Domestic wastes
     - 1.1.3. Food wastes
     - 1.1.4. Industrial wastes } in municipal
     - 1.1.5. Collected rainwater } water supply
   - 1.2. Industrial effluents fed directly into watercourses
   - 1.3. Chemical products used in water treatment
2. Diffuse sources
   - 2.1. Rural effluents
     - 2.1.1. Agricultural origin
       - 2.1.1.1. Soil erosion
       - 2.1.1.2. Irrigation water
       - 2.1.1.3. Fertilizer losses
       - 2.1.1.4. Domestic animal excrements
     - 2.1.2. Non-agricultural origin
       - 2.1.2.1. Organic forest wastes
       - 2.1.2.2. Wild animal excrements
   - 2.2. Springs and natural waters
   - 2.3. Inherent reserves in lakes
     - 2.3.1. Sediments
     - 2.3.2. Fauna and flora (biota)
     - 2.3.3. Water systems
   - 2.4. Atmosphere
     - 2.4.1. Rainwater
     - 2.4.2. Dust fallout

For simplification one can consider domestic effluents, *i.e.* municipal sewage, and diffuse rural wastewaters as being the two major sources of nutrients. In the case of the Federal Republic of Germany it can be assumed as a rough estimation that human excrements, detergents—these two together in domestic sewage—and influents of rural origin each supply about one third of the total contribution[31]. In individual cases the proportion of *e.g.* detergent phosphates can be higher —as in Lake Constance where this can be 30—40% higher[32]; in other cases *e.g.* in impounding reservoirs in country districts the proportion from rural wastewaters can predominate[33,34]. For Switzerland an overall contribution of around 30% from human excrements, 40% from detergents and 30% from the erosion of fertilized agricultural soils, including a small proportion from the natural weathering of rocks, has been quoted[35]. It is clear from such data that the problem of phosphorus in wastes must be regarded as a regional one, and that separate solutions have to be found for individual waters and regions.

1.4. Eutrophication Caused by Municipal Sewage

In those cases where the supply of phosphorus stems mainly from communal wastes, it is possible to combat eutrophication by extensive removal of this element. In the case of Lake Erie in North America, which was subjected to a detailed study, it was found that communal wastes accounted for some 59%[36] of the phosphorus entering the lake. A reduction of the phosphorus content in domestic wastes by 95%, in industrial effluents by 90%, and in wastewaters from rural areas by 60% was called for[37].

These values may deviate somewhat from those for other lake districts but they give a good indication of the sort of measures which must be taken. The removal of phosphorus from waters in rural areas is without doubt especially difficult, and its effectiveness is to some extent controversial. However, there is general agreement of opinion on the removal of phosphorus from sewage, as will be shown in the following sections.

2. State of Sewage Purification

2.1. Conventional Sewage Purification

Conventional methods for the purification of sewage consist essentially of physical, biological and, in special cases, chemical processes. Under the physical processes the principal step, usually a mechanical purification step, involves removal of debris and deposition of coarse impurities; under the biological processes we have the aerobic stage where, in this second step, the organic components of the sewage are degraded by bacteria[6]. The sludge precipitating in the mechanical and in the biological steps is usually further degraded and hygienically improved in an anaerobic step in a digester[6]. Such a conventional two-stage sewage purification results in an optically clear effluent which is practically free of suspended solids and has, for example, a maximum content of organic components corresponding to 20 mg BOD_5/l[*].

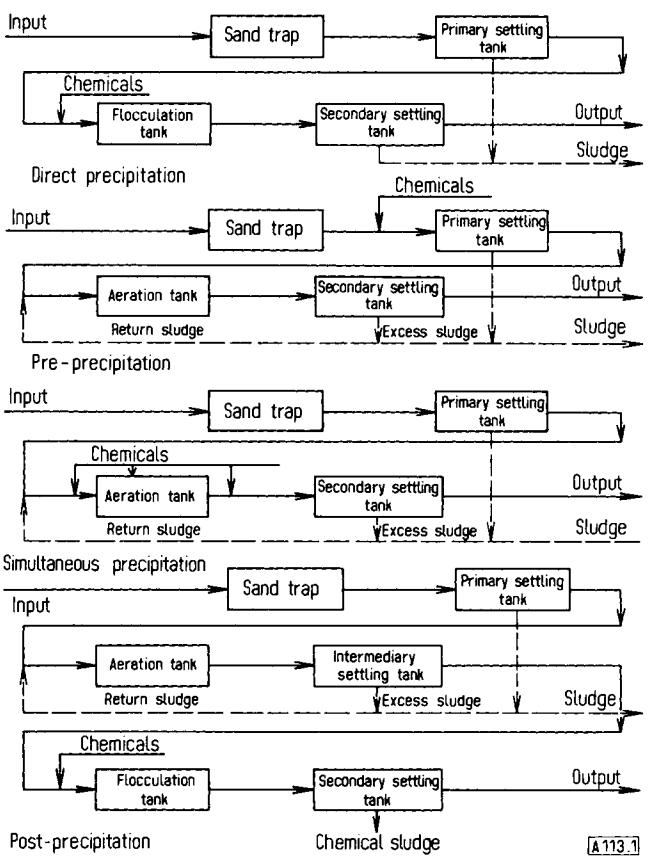

Fig. 1. Methods of precipitation purification for removal of phosphate. In direct precipitation, plant without biological purification steps are employed. For details see Section 3.1.7.

[*] BOD_5 (Biological Oxygen Demand in 5 days) denotes the amount of oxygen required for the oxidative degradation of the organic substances in the water in five days at 20°C in the dark. The amounts of organic constituents are expressed in mg BOD_5/l.

The increased consumption of water and the completion of canalization have led to increasing delivery of sewage to receiving waters. As outlined in the previous sections, recent examinations have shown that additional purification steps are necessary for removal of the nutrients phosphorus and nitrogen.

2.2. Additional Sewage Treatment

A suitable method for the removal of phosphorus is by precipitation as phosphates with iron, aluminum, or calcium salts (see Fig. 1). Methods, albeit expensive ones, have also been developed for the removal of nitrogen.

The greatest progress that has been made in recent years in the removal of phosphorus by precipitation has been in Sweden, where as long ago as 1974 the sewage from 50% of the population in densely populated areas passed through chemical or biological-chemical purification plant[38]. In the Great Lakes area of North America more than 200 sewage treatment plant include precipitation purification, in Switzerland *ca.* 70. Table 4 gives an overview of the sewage treatment plant already known to be in operation in the Federal Republic of Germany and which also incorporate a precipitation step.

Table 4. State of precipitation purification in the Federal Republic of Germany (see Fig. 1). 23 of the 25 precipitation purification plants are located near lakes and impounding reservoirs (for details see Section 3).

Precipitation method	Geographical region	Precipitant	Number of Plant
Direct precipitation	North	Al salts	1
Pre-precipitation	North	Al salts	3
	Central	Al salts, Al/Fe salts	6
	South	Al salts, lime + Fe salts	6
Simultaneous precipitation	North	Fe salts	2
	Central	Fe salts	2
	South	Al salts	4
Post-precipitation	North	Al salts	4
	South	Fe or Al salts	3
Unknown	Central	Fe salts	2
	South	Al salts	2

3. Phosphate Removal

3.1. Purification by Precipitation

3.1.1. Precipitants

The following compounds are commonly employed for the precipitation of phosphates from wastewaters: aluminum sulfate, aluminum chloride, calcium hydroxide, iron(II) sulfate, iron(III) chloride sulfate, and iron(III) chloride.

Because of their hygroscopic nature iron(III) salts are usually employed in dissolved form, whereas aluminum salts are also added in solid form, the products sometimes being granulated so as to facilitate dosage. Commercially available aluminum salts generally contain large amounts of iron. These precipitants are thus mixed precipitants. In precipitation purification the simultaneous employment of two precipitants is also occasionally resorted to[39]. It is often a matter of re-treated waste products or of compounds based on waste substances.

3.1.2. Chemical Aspects of Precipitation

A common feature of the precipitants mentioned is that they form sparingly soluble hydroxides and phosphates. During the precipitation hydroxide phosphates separate out, which according to estimated average M^{III}/P ratios of *ca.* 3:2 have the composition $[M^{III}(OH)]_3(PO_4)_2$[40,41]. Aluminum phosphate having the same Al/P ratio is found in Nature in the form of the mineral wavellite $Al_3(PO_4)_2(OH)_3 \cdot 5H_2O$. Precipitation with lime yields structures, which in their composition correspond to hydroxyapatite $Ca_5(PO_4)_3OH$[42]. Studies on aluminum hydroxide precipitation have proven, *inter alia*, the formation of an octanuclear complex[43], so polynuclear complexes are probably also formed in phosphate precipitation.

Among other things, it is assumed that the metal hydroxide initially formed in the precipitant solution exchanges hydroxide for phosphate ions on entering the phosphate-containing wastewater[44]. If the precipitant is first dissolved in water and then the phosphate-containing wastewater added to it, less phosphate is removed; this shows that the OH^-/PO_4^{3-} exchange proceeds relatively slowly. Under these conditions the hydroxide complexes and flocs have not only been completely formed but are also partially shielded by adsorbed substances. It may be assumed, therefore, that the phosphate is predominantly bound directly to the precipitant cations on rapid mixing with the wastewater. In addition phosphate ions are also removed by adsorption.

The degree of removal e is dependent on the relative amount of precipitant β (M:P), the phosphate content of the wastewater P_z, and the pH of the wastewater after precipitation.

$$e = k_1 + k_2 \log\beta + k_3 \log P_z - k_4\,\mathrm{pH}$$

On testing this equation experimentally, it was found that the results obtained agree satisfactorily (accuracy 5%) with those predicted. k_1, k_2, k_3, and k_4 are empirical constants[44].

The efficiency of the precipitant is dependent on the pH. For precipitation of orthophosphate, iron salts are most efficient at pH = 5, aluminum salts at pH = 6, and lime at pH > 10. Satisfactory removal of orthophosphate has, however, also been observed at pH values varying considerably from those just mentioned[40]. The solubility of the corresponding pure

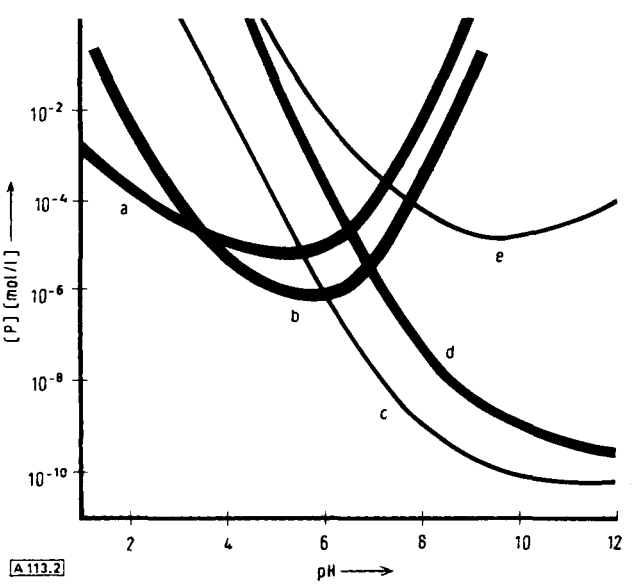

Fig. 2. Solubility of phosphates as a function of pH. a) $FePO_4$, b) $AlPO_4$, c) $Ca_{10}(PO_4)_6F_2$, d) $Ca_{10}(PO_4)_6(OH)_2$, e) $Ca_4H(PO_4)_3$.

phosphates is also at its lowest at the above pH values[45] (Fig. 2).

3.1.3. Orthophosphate and Condensed Phosphates

Domestic wastes contain both inorganic and organic phosphorus compounds. 85—90 % of the phosphorus compounds are of an inorganic nature[40]. These consist predominantly of orthophosphates, since any condensed phosphates also entering the wastewater are partially hydrolyzed before reaching the purification plant[46]. Hydrolysis continues in the purification plant. *Lewin* found that the proportion of condensed phosphates in raw sewage amounted to about 20 %, while no condensed phosphates were present in the water after treatment[47]. Investigations carried out on raw sewage to a communal purification plant yielded the distribution of phosphates listed in Table 5, according to which a considerable portion of the phosphates are already hydrolyzed to phosphate in the preliminary clarification tanks.

Table 5. Distribution of phosphates in the effluent of a sewage treatment plant (P content in mg/l). The plant is designed for a PE of *ca.* 10000 (PE = "population equivalent").

	Total	Orthophosphate	Condensed phosphates			
			Diphosphate	Triphosphate	Others	Σ
Raw sewage						
unfiltered	36.2					
filtered	15.9	10.2	0.7	4.1	0.9	5.7
undissolved	20.3					
Effluent of primary settler						
unfiltered	30.1					
filtered	23.3	21.6	0.35	0.65	0.7	1.7
undissolved	6.8					

The condensed phosphates present are mainly the pentasodium triphosphate $Na_5P_3O_{10}$ arising from detergents, along with tetrasodium diphosphate and higher condensed phosphates.

Condensed phosphates—so far as they are still not hydrolyzed—are precipitated directly, like orthophosphate[40]. The removal of individual condensed phosphates varies according to the pH (Fig. 3).

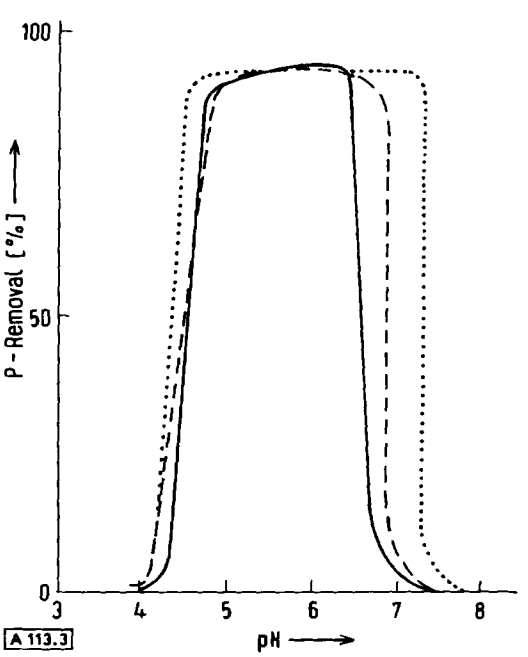

Fig. 3. Removal of condensed phosphates with aluminum sulfate as a function of pH. —— diphosphate, – – – triphosphate, ····· higher condensed phosphates. The pH after precipitation is given.

These diagrams give no indication that the precipitation of condensed phosphates is connected with simultaneous hydrolysis. In the precipitation the degree of removal of triphosphate and orthophosphate is about the same, while under the same conditions it is lower by 5—10 % in the case of diphosphate and by 10—15 % in the case of metaphosphate[48].

It can be assumed that a part of the organically bound phosphorus is also precipitated by adsorption on the flocs. These compounds are converted into inorganic phosphates in the biological purification step, whereupon hydrolysis of the condensed phosphates is also completed at the same time[46].

3.1.4. Amount of Precipitant Required

The molar ratio of aluminum and iron(III) to phosphorus necessary for more than 90 % precipitation of orthophosphate has been reported to be M:P = 1.4:1[41]. In practice ratios up to 2.0:1 are found[40], thus indicating the prevalent undesired precipitation of pure hydroxides. When the optimum amount of precipitant is used, the content of its cations in the effluent is not higher than in the untreated raw sewage input. In the case of simultaneous precipitation (see Fig. 1) with iron salts, *Leumann*[49] found an average of 0.714 mg Fe/l in the effluent compared with 0.206 mg Fe/l in the raw sewage. Similar ratios were found on precipitation with aluminum salts[50].

Higher contents of precipitant cations in the effluent than in the feed are indicative of the presence of complexing agents such as nitrilotriacetic acid, whereby the demand on precipitant is increased[51]. As has already been shown in an OECD survey (Table 6)[52], precipitation with calcium hydroxide requires considerably larger amounts of precipitant than are required in the precipitation with aluminum or iron(III) compounds.

3.1.5. Degree of Phosphate Removal

At a constant M^{III} : P molecular ratio the degree of P removal with a commercial aluminum sulfate/iron(III) sulfate precipitant increases with increasing initial content of phosphorus (Fig. 4). The poorer removal of phosphorus at lower concentration than at higher concentration can be compensated only in part by increasing the amount of precipitant (Fig. 5). In direct comparison with iron(III) chloride, aluminum sulfate gave by far the better degree of phosphate removal[53].

Table 6. Dosage of precipitant and optimum pH ranges for precipitation [52].

Method of precipitation	Al	Fe^{III}	Ca
Pre-precipitation			
Dosage [g/m³]	6—12	10—25	100—150
pH	6—7	≈ 5	>9.5
Simultaneous precipitation			
Dosage [g/m³]	6—10	6—20	—
pH	5.5—7.0	5—7	—
Post-precipitation			
Dosage [g/m³]	6—12	10—25	180—425
pH	5.5—7.5	5	11.5

3.1.6. Flocculation

Separation of the precipitated phosphate is dependent on floc formation. Hydroxide phosphates are initially formed as very small particles which separate only when the zeta potential tends towards zero.

Floc formation and the amount of precipitant required are thus influenced by the ions present in the wastewater. A high zeta potential can be more advantageously reduced by addition of polyelectrolytes than by overdosage of precipitant because the system then leaves the range of pH favorable for flocculation[40].

Destabilization and transport of the colloids requires energy; this can be supplied by stirring. Particular attention must be paid, however, to the velocity gradients in the reaction vessel[54].

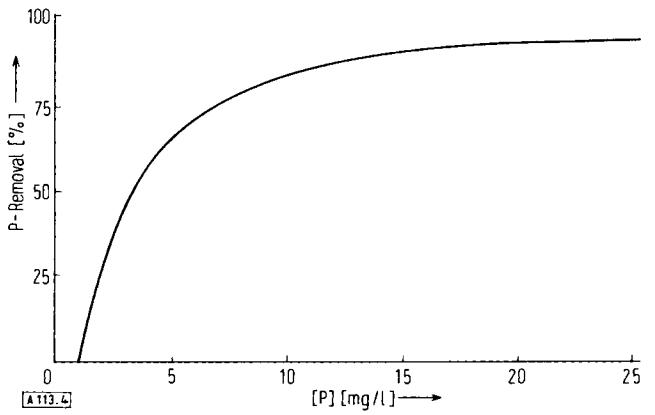

Fig. 4. Phosphate removal at constant pH (after precipitation 6.5±0.3) and constant M^{III}:P ratio (1.6:1).

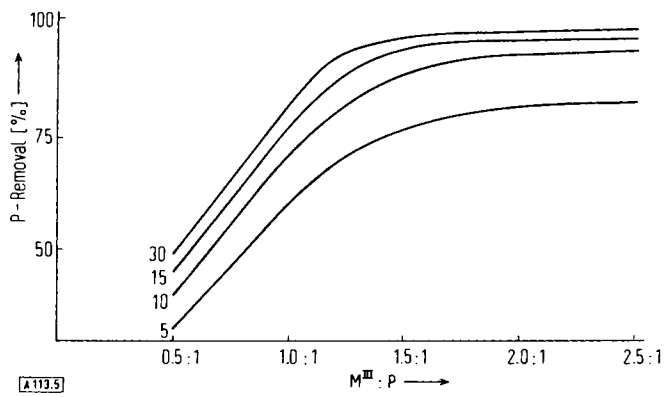

Fig. 5. Phosphate removal as a function of the M^{III}:P ratio and of the initial concentration (given in mg P/l). pH after precipitation 6.5±0.2; mains water with 14° hardness (German scale).

The hardness of the water has only a slight influence on the precipitation. Floc formation is somewhat improved with increasing hardness, and the drop in pH on addition of precipitant is smaller. Ca ions also participate in the precipitation of phosphate, but without notable influence however on the degree of removal observed in laboratory experiments with 15 mg P/l and water hardnesses between 0 and 20° (German scale). The precipitant flocs adsorb colloids; hence other sewage components are removed at the same time as phosphates [organic compounds (expressed as BOD_5), chemically oxidizable compounds (expressed as chemical oxygen demand, COD), heavy metals]. This effect is an essential factor in the assessment of precipitation as a general method for the purification of wastewaters (see Section 4.2).

3.1.7. Possible Incorporation of Precipitation in Sewage Treatment Plants

Purification by precipitation for the removal of phosphate can be carried out in existing one- or two-stage sewage treatment plants under favorable conditions without need for further installations. In some cases, however, construction of a separate "third purification step" is recommended.

In precipitation purification one distinguishes between three processes: pre-precipitation, simultaneous-precipitation, and post-precipitation (the names signify the point at which the precipitation is carried out referred to the biological stage). Pre- and simultaneous-precipitation (Fig. 1) can be employed directly in existing sewage treatment plants; post-precipitation requires incorporation of an additional step in the plant. Sewage purification by precipitation without biological processes is referred to as direct precipitation. Removal of phosphate with aluminum and iron(III) compounds can amount to ≥90% in all the methods quoted. In simultaneous-precipitation the average removal is only 5% less, probably because the phosphates liberated in the mineralization of organic phosphorus compounds are no longer completely collected by the precipitant flocs formed in the feed to the aeration tanks; this disadvantage can be avoided by addition of precipitant to the aeration tank or trickle filter discharge with the usual return sludge ("hybrid precipitation"). With iron(II) sulfate, on the other hand, only *ca.* 80% of the phosphorus is removed in practice in the case of simultaneous precipitation[55].

Pre-precipitation has the advantage that it is less demanding on the biological step since about 60% of the organic compounds (BOD_5load) have already been removed. Moreover, heavy metals, which can have a toxic action on biological degradation, and other toxic substances are removed prior to the biological step. The advantages of post-precipitation lie in the fact that good formation of flocs is guaranteed by optimal mixing in a separate flocculation tank. The results of post-precipitation surpass those of the other methods. Very low phosphate and BOD_5 can be achieved. Irregularities in the previous purification steps can be largely compensated for in post-precipitation. The flocs are separated by sedimentation, flotation or filtration.

3.1.8. Feed and Amount of Precipitants

The precipitants are added either in solid form or in solution. A rapid and intimate mixing of the components must result, and sufficient residence time allowed for floc enlargement.

Flocculation tanks furnished with slow moving stirrers enable adequate agitation for enhanced floc formation. The sewage passes through several flocculation tanks whose stirrers are adjusted to run stepwise at rates ranging from about 0.3 to 0.1 m/s. The overall residence time of the sewage in the flocculation tanks should be about 20—30 minutes.

Flocculation tanks are not available in some existing sewage treatment plants for the incorporation of precipitation purification as *e.g.* pre- or simultaneous precipitation. In these cases a suitable feedpoint in the plant must be sought at which requisite motion of sewage for thorough mixing and for formation of readily settleable flocs is fulfilled. If necessary this motion is effected by installation of extra equipment or by altering the feed of water. Solutions of commercially available precipitants are generally corrosive. The materials used in the construction of plant must therefore be corrosion-resistant. Consequently, the storage and transport of dissolved precipitants are more costly than in the case of solid precipitants, some of which can be transported and stored in normal sheet-steel tanks.

The dosage can be controlled electronically according to various parameters. A simple method of control geared to the amount of feedwater is frequently adopted. Regulation of the dosage according to phosphate loading entails incorporation of an automatic analyzer by means of which the feedwater value is superimposed with a phosphorus value[56]. About 30% of precipitant can be saved in this way and the amount of sludge is also reduced[57].

3.1.9. Separation of Precipitated Sludge

The efficacy of precipitation purification is essentially determined by the separation of the flocs. In pre-precipitation they are separated by sedimentation in preliminary settling tanks. Precipitation purification in the activated sludge step (simultaneous precipitation) usually has a favorable influence on the simultaneous settling of activated sludge in the second or final settling tank. Separation is then possible by flotation, aerated water being added to the sewage so that the flocs float. The sludge separated in this way has a solids content

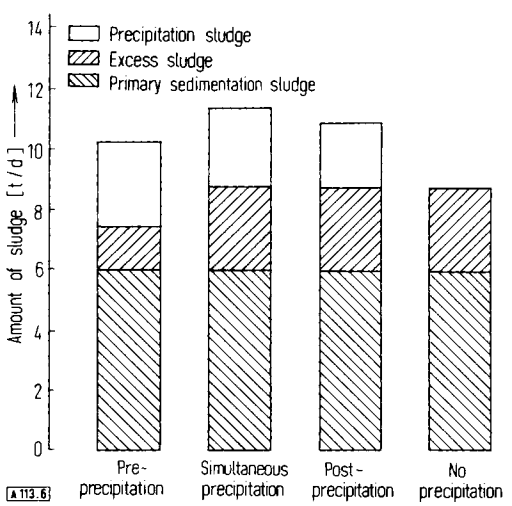

Fig. 6. Precipitated sludge in various precipitation methods. The "excess sludge" is the sludge produced in each case in the activated sludge step (in the aeration tank). The data are for a PE ("population equivalent") of 100000.

three-to fourfold that of sedimented sludge. A flotation tank requires about a third of the area required for a sedimentation tank[58].

When used in solid form, aluminum and iron salts are present as hydrates. The dry solid from the precipitated phosphates has a weight still amounting to only *ca.* 50% that of the precipitant employed, since the dry phosphates are essentially not hydrated. The situation is much different in the case of precipitation with CaO, which alone increases in weight *via* uptake of anions, and the weight of dried solid matter finally amounts to *ca.* 150% that of the starting weight.

The total volume of sludge occurring in a mechanical-biological sewage treatment plant is increased by about 30—50% by precipitation with an essentially unchanged preliminary sludge solids content of 3%[50]. (For details of simultaneous- and post-precipitation see Refs. [59, 60].) The amounts of sludge produced in each of the precipitation methods are compared in Figure 6.

The following increases in dry solids in sludge compared to that in mechanical-biological wastewater purification has been quoted: pre-precipitation 16%, simultaneous precipitation 34%, post-precipitation 28%[40]. Mixed sludges occur in pre- and simultaneous precipitation, a fact that must be taken into consideration in any further treatment. Lime, for example, may not be employed if the sludge is to be subsequently digested.

3.1.10. Handling of Sludges

Sludges obtained by precipitation with aluminum and iron salts do not disturb the processes of dehydration or of stabilization from a biological viewpoint on admixture with primary settler or biological excess sludge. A stabilization (aerobic or anaerobic) of the separable post-precipitation sludge is not necessary, since the proportion of organic matter is small[40]. The post-precipitation sludge can be admixed with the digested, *i.e.* the anaerobically stabilized, sludge to improve the dehydration properties.

Theoretically, the anaerobic stabilization of sewage sludges involves the danger of re-dissolution of the precipitated phosphate, particularly from the iron hydroxide phosphate flocs. However, *Thomas*[61] did not observe any deviations in the content of phosphate in discharge water from a sewage treatment plant after periodic addition of digester effluent. According to other studies the proportion of dissolved phosphates in the digester effluent also remains small on employing precipitation purification[49]. Liberation of phosphate by sulfide ions formed under anaerobic conditions is also considerably suppressed by calcium ions[62]. Besides anaerobic stabilization, an aerobic or a chemical stabilization (with lime) also finds use in sewage sludges. Stabilization is unnecessary in sludge incineration, which can be carried out independently, if necessary with refuse, after dehydration to $\geqq 30\%$ dry solids. Before disposal of sludges, stabilization and dehydration (40% dry solids) as well as a check on the dumping ground is necessary.

Stabilized and thickened sewage sludges can be used agriculturally. The phosphate in precipitation (mixed) sludges is especially useful as a nutrient for plants; in a mixed sludge obtained on precipitation with aluminum sulfate 75% of phosphate soluble in citric acid at a total-P_2O_5 content of 13% was found, in a secondary sewage sludge 70% citric acid solubility

at 28 % total-P_2O_5. Since heavy metals are entrained on precipitation their content in the mixed sludge increases (Table 7). *Anderson* and *Nilson*[63] investigated the extent to which the heavy metals of the sewage sludge are taken up by soil and by vegetation (Table 8).

Table 7. Heavy metals in primary sedimentation sludge (2 % dry solids) of a sewage treatment plant.

	Without precipitation [ppm]	Pre precipitation [ppm]
Fe	380	396
Zn	36	61
Mn	7.0	16.0
Pb	4.0	8.0
Cu	2.0	6.0
Cr	1.6	2.0
Ni	1.0	1.5
Cd	<0.1	0.2
Hg	0.1	0.2

duction was determined *via* the protein content. A reduction of more than 50 % in algal growth in the effluent compared to that in the feed could be detected at dilutions of 1:25 onwards with phosphorus-free nutrient solution NAAM[64].

The decrease from 3.8 to 0.9 mg P/l at the dilutions 1:25 and 1:50 produces at least the same decrease in growth again as that from 24.2 to 3.8 mg P/l. These dilution factors, which resemble natural ratios, gave concentrations nearly the same as that claimed by *Sawyer*[28] (Table 9).

3.1.12. Costs

The human being excretes about 1.7 g of phosphorus per day[65]. Together with a similarly high contribution from washing and cleansing agents, and taking into consideration other household wastes, the daily release of phosphorus into domestic sewage can be assumed to be 4 g per inhabitant. The precipitants frequently employed in sewage treatment in the Federal Republic of Germany cost DM 0.06 to 0.08/mol Al

Table 8. Analytical data for trace elements. Content in the sewage sludge. Relative mean values for soils and vegetation, and contents after using sewage sludge [63]. S = solid matter.

Element	Content in sewage sludge [µg/g S]	Content in soil Rel. mean value [µg/g S]	Content in soil after sludge usage [µg/g S]	Content in vegetation Rel. mean value [µg/g S]	Content in vegetation after sludge usage [µg/g S]
Mn	373	476	480.0	35.7	40.8
Zn	4890	97.9	368.8	34.3	114.5
Cu	1960	25.5	90.5	3.9	8.3
Ni	88	28.2	43.3	4.9	9.2
Co	12.2	14.2	14.6	1.6	1.9
Cr	176	36.1	61.0	2.6	4.1
Pb	293	25.7	43.9	5.2	7.7
Cd	11.0	1.2	1.7	0.6	0.6
Hg	12.0	0.018	0.675	0.033	0.049
Mo	7.4	0.53	0.68	1.1	1.7
As	6.6	12.3	12.5	0.37	0.73
B	30	0.59	0.76	29.1	35.7
Se	7.3	0.238	0.569	0.07	0.06

3.1.11. Algological Tests

With regard to eutrophication it is of interest to assess the nutrient potential of a treated sewage, especially for algae; a simple correlation with the concentrations of constituents cannot be established in each and every case. A suitable method for evaluating the nutrient potential is the Algal Assay Procedure (AAP)[12] in the form of the "Bottle Test". The AAP was first developed in the USA for estimating the degree of eutrophication of receiving waters, and specifies, *inter alia*, the test algae to be employed: *Selenastrum capricornutum* (green alga), *Anabaena flos-aquae* and *Microcystis aeruginosa* (blue-green algae), and a diatomaceae still to be named. A further component of the AAP is the nutrient solution, the New Algal Assay Medium (NAAM, Table 2)[12].

A modified method was used for testing effluents from sewage treatment plant after adequate dilution. The alga pro-

or Fe^{III}. At a molar ratio M:P of 1.4:1 the cost for precipitants would be DM 0.013 per day or DM 4.75 per year per inhabitant. Since *ca.* 30 % of the phosphates are already separated off in the mechanical and biological stages of the sewage treatment plant without precipitation the theoretical cost reduces to DM 3.10 per year per inhabitant. The actual average values quoted in the literature lie somewhat lower. Total operational costs are on average about double those for precipitants (Table 10).

3.2. Ion-Exchange

Exchange resins in the OH or Cl form are used for the removal of phosphate by ion-exchange, the OH form being preferred for the removal of anions. According to *Wagner*[66] residual phosphate contents of 0.5 mg/l are found in the

Table 9. Growth of *Anabaena flos-aquae* in wastewaters at dilutions of 1:25 and 1:50.

	P content [mg/l]	P content [%]	Algal growth [%] 1:25	Algal growth [%] 1:50	P content [mg/l] 1:25	P content [mg/l] 1:50
Raw wastewater	24.2	100	100	100	0.97	0.48
Effluent of primary settler	3.8	16	70	70	0.152	0.076
Effluent of secondary settler	0.9	4	34	36	0.036	0.018

Table 10. Cost of precipitation purification. PE = population equivalent; I = inhabitant.

Connected load	Precipitant	Yearly cost of precipants	Yearly operating costs	Remarks	Ref.
5000 to 22000 PE	$FeClSO_4$	2.00 to 3.50 Sfr PE average 2.75 Sfr PE		simultaneous precipitation 8 plant	[49]
ca. 5000 to 100000 PE				simultaneous precipitation 17 plant	[49]
50000 I	FE^{III}	4.25 Sfr/I	5.45 Sfr/I	simultaneous precipitation	[90]
400 l l^{-1} d^{-1}	(25 mg/l)			(estimated)	
50000 I	Fe^{III}				
400 l l^{-1} d^{-1}	(10 mg/l) $Ca(OH)_2$ (120 mg/l)	3.80 Sfr/I	7.15 Sfr/I	post-precipitation (estimated)	[90]
8000 to 150000 PE	Al(Fe) sulfate	1.95 to 3.26 DM/PE		pre-precipitation 6 plant	[102]
13000 to 33000 PE		0.97—3.85 DM/PE		post-precipitation 3 plant	[102]
30000 PE		2.12 DM/PE		direct precipitation 1 plant	[102]
10000 PE	Lime	0.95 $/PE	4.60 $/PE	pre-precipitation	[52]
	Alum.	0.78 $/PE	4.20 $/PE		
	$FeCl_3$	0.78 $/PE	4.20 $/PE		
150000 PE		2.00 DM/I	3.50 DM/I	pre- or simultaneous precipitation	[103]

effluent. The advantage of this method of purification lies in the fact that no initial concentrations have to be measured for optimum control of the process. Measurements of conductivity in the effluent and the possibility of switching over to a second system, which is constantly loaded or regenerated, suffice.

Disadvantageous for converting to this method in practice is the cost of the excess regenerants that are required. The volumes of washer water necessary can amount to 20% of the volume of wastewater to be purified[67]. The regenerates are concentrated solutions of pollutants and must be further treated, whereby the phosphates are expediently removed by precipitation[68]. The exchange materials in use up to the present are not specific. Besides phosphates other anions (SO_4^{2-}, NO_3^-) and organic substances (BOD_5, COD) are also adsorbed or exchanged, and hence the exchange capacity is reduced. It is for these reasons that this purification step has so far not been incorporated in the treatment of municipal sewage.

3.3. Biological-Chemical and Biological Processes

Aerobic biological steps as carried out in activated sludge systems or trickle filter plant aid the microbial respiration of organic sewage components, which in wastewater engineering are measured according to the biological oxygen demand (BOD_5). The biological step not only requires oxygen but also nitrogen and phosphorus as well as trace elements for the maintenance of vital bacterial functions. In a complete sewage treatment plant up to 70% of the dissolved phosphorus in sludge can be converted or adsorbed[69-71].

A number of processes for the removal of phosphorus exploit this effect in that a part of the activated sludge is separated off and further processed under anaerobic conditions. The sludge releases bound phosphate into the overlying liquid, which is separated from the sludge and, *e.g.*, once again subjected to chemical precipitation. In the "Pho-Strip" process[72] lime is used for the precipitation[73]. In the "Bardenpho" process[74] up to 90% of the phosphates are separated biologically. In another process that has been proposed the phosphate from the digester water is separated by warming[75], whereupon a highly nourishing fertilizer, magnesium ammonium phosphate, is precipitated in the presence of magnesium ions.

According to *Bringmann*[76], the water is separated from the sludge after passing the biological step and fed over two biological filters with PVC beads as substrate, whereby it is dosed with Fe^{2+} ions and CO_2. Up to 99.99% P is removed; the residual value of P in the effluent is 0.007 mg/l[77].

According to these results removal of P and its embodiment in a biomass is indeed possible, but since the phosphorus thus bound is remobilizable under anaerobic conditions an absolutely quantitative fixation might here also be possible only by chemical precipitation.

Consequently, these biological processes enable only a concentration of the phosphorus and must be finally supplemented by precipitation purification. Finally, for the biological removal of phosphates other methods are also recommended which can be utilized according to the actual sewage treatment process itself. These include the cultivation of algae ("high rate algal pond system")[78] or of the sedge *Scirpus lacustris*[79] in ponds, as well as the irrigation of, if necessary only mechanically pretreated, sewage on used agricultural and forestry areas[80]. Prerequisite for the latter mentioned methods are suitable local and climatic conditions, so it is doubtful that they will find universal application.

4. Removal of Other Pollutants

4.1. Nitrogen

4.1.1. Oxidation and Reduction Processes

Nitrogen can be present in several forms of combination in waste-waters. Formally negatively charged nitrogen is predominantly present in the form of ammonia or ammonium salts and amines *e.g.* amino acids and urea. Urea, of which the human being excretes about 30 g daily in urine, represents the most important source of nitrogen in municipal sewage[81]. Microbial hydrolysis and subsequent oxidation leads initially

to formation of ammonium ions and then to nitrite and nitrate. Nitrogen in the form of the nitrate is toxic to human beings, which can make itself noticeable in small children as "cyanosis"[82,83]. In the conventional sewage treatment process only up to 20% of the nitrogen is removed, since it does not readily form insoluble compounds (no sedimentation during the preliminary clarification) and in the aerobic biological step only a small part is required for degradation of the biomass. In wastewater treatment the bacterial oxidation of ammonia nitrogen to nitrate in the presence of excess oxygen is referred to as nitrification[6]. In the presence of excess resorbable carbon (BOD_5 carrier) and a deficiency of oxygen, on the other hand, the energy metabolism of aerobic bacteria is, according to *Wuhrmann*[84], so maintained that NO_3^- or NO_2^- function as electron donors in the respiratory chain. N_2 and/or N_2O are formed as final products and are released into the atmosphere in gaseous form. This reduction (denitrification) takes place very rapidly.

4.1.2. Processes for Removal of Nitrogen

Suitable processes for the removal of nitrogen from wastewater on a technical scale are listed in Table 11[85].

Table 11. Processes for removal of nitrogen.

1. Physical processes	Distillation
	Reversed osmosis
	Filtration
2. Chemical and chemical-physical processes	Ammonia stripping
	Ion-exchange
	oxidation, reduction
	Electrodialysis
	Sorption
	Electrochemical processes
3. Biological processes	Embodiment in biomass
	Anaerobic denitrification

Use of the purely physical processes has so far been very limited because of the high investment and energy costs that are generally involved.

Ammonia nitrogen can be removed almost quantitatively in an alkaline environment at pH = 9 to 12 by aeration of the wastewater; for example, up to 98% is removed at pH = 10.8 by passage of *ca.* 3 m^3 air/m^3 wastewater[86]. The ammonia is subsequently adsorbed and neutralized. However, considerable energy, reagent, and investment costs have discouraged application of this method on a large scale. The use of ion-exchangers is also costly owing to the frequent succession of regenerations called for (see Section 3.2).

An attractive method would appear to be that in which NH_4^+ and PO_4^{3-} ions are each exchanged to about 90% simultaneously on zeolites[87]. Regeneration of the zeolite is carried out with $Ca(OH)_2$ solution. Electrodialysis and sorption on activated charcoal for the removal of nitrogen from municipal sewage are at present likewise to be regarded as special methods which are not employed in practice. Moreover, these process steps are primarily intended for the removal of other sewage constituents.

In a process developed in Norway ammonia nitrogen and phosphate ions are each removed to the extent of 82% in one step. The raw sewage is mixed with seawater in an electrolytic cell and electrolyzed at carbon electrodes. This leads to evolution of hydrogen and precipitation of $Ca_3(PO_4)_2$, $MgNH_4PO_4$ and $Mg(OH)_2$, which are subsequently separated by flotation. A byproduct is chlorine, which can be utilized for disinfecting the effluent[88].

In biological processes, bacterially controlled redox reactions are also used in practice for the removal of nitrogen (see Section 4.1.1). According to *Wuhrmann*[89,90,84] the process operates according to the following scheme:

$$\text{NH-compounds} \xrightarrow[\text{microbial oxidation}]{\text{"nitrification"}} NO_2^-, NO_3^- \xrightarrow[\text{microbial reduction}]{\text{"denitrification"}} N_2 \longrightarrow \text{atmosphere}$$

Microbial reduction, an anaerobic metabolism, proceeds satisfactorily only in the presence of sufficient resorbable carbon, which *e.g.* according to *Jeris*[91] is derived from methanol, in order to bring the C:N molar ratio of 2:1 in the sewage to the known optimum value of 7.7:1[92,93]. Thereby nitrate nitrogen can be removed by up to 99%[93].

Despite the additional investment involved, anaerobic denitrification is the most economical possibility for the removal of nitrogen. The process does not exhibit any marked dependence upon temperature and avoids the disadvantage of embodiment of nutrients in biomasses from which they are able to be remobilized[84].

4.2. Heavy Metals and Organic Substances

During the precipitation of phosphates heavy metals are entrapped by the hydroxide phosphate flocs ("collector precipitation"[94]). Hence, in the sludge from the sewage treatment plant the contents of the frequently occurring elements Zn, Mn, Pb and Cu can double and those of Cr, Ni, Cd and Hg increase[95], such that effluents from precipitation plant finally contain only residual quantities of the order of 0.1 mg/l[96] or smaller[48]. Complexing agents interfere with heavy metal precipitation. On addition of 0.025 mmol nitrilotriacetate/l the total content of copper in solution (0.025 mmol/l) during the purification by precipitation remains unchanged, otherwise it would be reduced to less than 0.001 mmol/l[51].

Organic constituents of sewage, expressed as biological (BOD_5) or chemical oxygen demand (COD), also separate out during purification by precipitation. The removal of BOD_5 in the primary settling tank increases from 30% without precipitation to 60% with precipitation, that of COD from 25% to 43%; the corresponding values in the secondary settling tank are 94 to 96% and 72 to 80%, respectively[97]. The effect can be exploited for increasing the efficiency of overloaded biological treatment steps (Table 12).

Table 12. Removal of waste water constituents with and without precipitation purification; precipitation with Al- or Fe salts. Data in % [50]. Data for mechanical-biological purification without precipitation are given for comparison.

	Pre-precipitation		Simultaneous precipitation		Direct precipitation		For comparison
	Precipitant						
	Al	Fe	Al	Fe	Al	Fe	—
P	99	97	94	93	98	97	10
BOD_5	99	93	88	83	77	60	94
COD	91	84	74	60	59	55	67

5. Limitations of the Processes and Alternative Suggestions for Additional Wastewater Treatment

5.1. Recycling in the Water Systems

Even extensive employment of phosphate precipitation in all cases where a stagnant or slowly running water contains phosphorus primarily originating from sewage does not guarantee prevention of eutrophication. Apart from the entry of phosphate from diffuse sources consideration must above all be also given to the receiving water's own reserves of phosphorus in the sediment[98]. Thus, in the case of a lake in Wisconsin no reduction in algal growth was observed after complete restraint of entry sewage[99]. In 1972 a high phosphorus content was measured in Lake Vierwaldstätter which was ascribed to redissolution of phosphate from the sediment due to oxygen difficiency in the depths of the lake. Such redissolution processes have already occurred earlier, before loading of the lake with municipal sewage constituents was put into operation[100]. Recycling also sets in, when dead algae sink to the bed and once again release nutrient elements as a result of bacterial decomposition processes.

5.2. Replacement of Wastewater Components

The onerous concentrations of phosphorus, nitrogen, heavy metals, organic substances *etc.* in sewage allowed to enter receiving waters leads to the question whether this can be remedied by altering the composition of the sewage. In this connection it is considered essential to limit the content of phosphate in detergents. According to the "Law on the Environmental Compatability of Washing and Cleansing Agents" ("Detergent Law"), which came into force on September 1, 1975, legal rulings for the restricted use of phosphates in washing and cleansing agents can be enacted[101]. However, complete removal of the phosphate from detergents is also no decisive remedy, since the contribution of detergent phosphates in municipal sewage varies locally and amounts to no more than 60% even in densely populated areas where there is positive control on phosphate from human excrements. The remaining contribution from human excrements still leads to an accelerated algal growth[36], so phosphate precipitation must be implemented in any case. The problems associated with incorporating other substances in detergents instead of phosphates have already been dealt with elsewhere[102, 31].

6. Conclusion

The causes of accelerated eutrophication, *i.e.* the increasingly observed over-fertilization, especially of stagnant and slowly flowing waters, in the past few years mainly stem from the impact of civilization. Insofar as the influence of canalized municipal sewage predominates over those of diffuse sources the most recommendable measures that can be taken at present to combat eutrophication is the implementation of phosphate precipitation in sewage treatment plant. The effluent from treatment plant must be so effectively freed from phosphorus that it will always be the growth determining factor after adequate dilution in surface waters. In this way longer term contributions can be made toward the sanitation of waters; at the same time retarding factors such as the contribution of diffuse sources and internal recycling in the water systems must be taken into consideration.

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COMMUNICATIONS

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

Benzo[14]annulene[1]

By *Ute E. Meissner*, *Annelies Gensler*, and *Heinz A. Staab*[*]

Since 1965 we have been investigating a series of [4*n*]- and [4*n*+2]annulenes annelated with benzenoid systems[1, 2], the aim of our studies being "to ascertain the extent to which nonbenzenoid macrocyclic conjugation is capable of prevailing over π-electron interaction within benzenoid subunits"[2b]. This concept has meanwhile attracted the attention of other research groups, too, interested in assessing the relation of benzenoid to nonbenzenoid aromaticity[3, 4]. Although benzo[14]annulene systems have been included in these studies[4], the parent system itself has so far not been obtained. We now report the synthesis of benzo[14]annulene.

Double Wittig-reaction (*n*-butyllithium, tetrahydrofuran, −35 °C) of 1,2-bis(triphenylphosphoniomethyl)benzene dibromide with 4-pentynal gave a mixture of *cis/trans* isomers of 1,2-bis(1-hexen-5-ynyl)benzene, from which the *trans-trans* isomer *(1)*[5] was isolated (m.p. 31—32 °C, from methanol; 15% yield) by column chromatography (silica gel, CCl_4). Cyclization of *(1)* with copper(II) acetate in dimethylformamide[1] afforded the 14-membered ring system *(2)* (m.p. 115—117 °C, from ethanol; yield 48%)[5] from which benzo[14]annulene [m.p. 106—108 °C, from ligroin (60—70 °C); yield 9%][5] was obtained by isomerization with potassium *tert*-butoxide in *tert*-butanol/benzene.

According to ^{1}H-NMR *(vide infra)* the compound obtained is not *(4)*, but *(5)*, which differs from *(4)* in the sequence of double bonds in the 14-membered ring [*(4)*: *ctcttct*; *(5)*: *ctctctt*]. Compound *(4)*, in which coplanarity ought to be more strongly hindered than in *(5)* due to short H···H distances corresponding to *o,o'*-interactions in biphenyl, could

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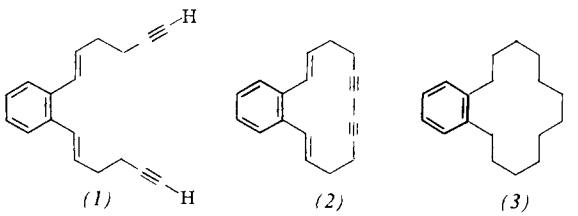
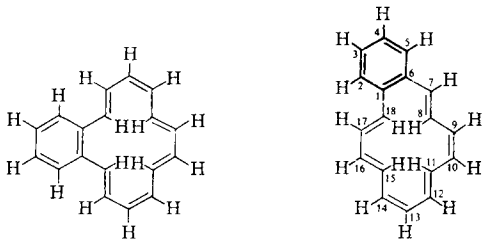
not be detected. Hydrogenation of *(5)* with Pd/activated charcoal in benzene gave *(3)*[5], identical with the hydrogenation product of *(2)* obtained under the same conditions (m.p. 58.5—59 °C; 58—59 °C[6]).



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



(4) *(5)*

In the UV spectrum, the transition from the non-conjugated precursors *(1)* and *(2)* to the cyclo-conjugated *(5)* is characterized by a strong bathochromic shift together with an increase in the extinction [*(1)*: λ_{max} = 233.5 nm ($\log\varepsilon$ = 4.391, 260 (4.257); *(2)*: 234 (4.348), 255 (sh, 4.076), in ethanol; *(5)*: 305 (4.703), 360 (sh, 3.666), in cyclohexane].

The ^{1}H-NMR spectrum (220 MHz, CS_2)[7] of *(5)* shows a 1H absorption around δ = 7.7, a further 1H absorption around δ = 7.4, and a 2H multiplet around δ = 7.3. These signals are assigned to the "aromatic" protons H-2, H-5, and H-3/H-4. In addition the spectrum contains a group of signals for eight H-atoms between δ = 7.1 and 6.25 and a further group for four H-atoms between δ = 5.2 and 4.3. The former is assigned to the outer, the latter to the inner protons. This assignment is supported by the fact that a 1H "doublet" with $J \approx 16$ Hz is observed within each of these groups at lowest field strength; they are to be ascribed to the two protons (H-18, H-7) in the α-positions to the benzene ring, one of which (δ = 5.12) is inside, the other (δ = 7.05) on the periphery of the [14]annulene system. This finding as well as the mentioned resonance pattern of the "aromatic" protons, rules out the symmetric structure *(4)*. The difference of 1.93 ppm between the inner and outer α-H absorptions and the upfield, respectively downfield shift as compared to the two equivalent α-H atoms in the nonconjugated precursor *(2)* [+1.51 ppm for the inner H-18, −0.42 ppm for the outer H-7], together with the splitting of the "non-aromatic" protons into a group of eight outer and a group of four inner protons, reveals the diatropic character of the 14-membered ring system in *(5)*. However, as in the [18]annulene series[1,2c], in [14]annulene, too, the induction of a diamagnetic ring current is considerably weakened by the condensation with a benzene ring.

Measurements of the ^{1}H-NMR absorption (220 MHz, hexachlorobutadiene) up to 110 °C do not show the formation of other conformations of *(5)*. With increasing temperature the signals of the inner protons are, however, shifted to lower field (up to −0.25 ppm), those of the outer protons to higher field (up to +0.08 ppm).

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CAS Registry numbers:
(1), 58673-22-6; *(2)*, 58673-23-7; *(3)*, 58673-24-8; *(5)*, 58673-25-9; 1,2-bis(triphenylphosphoniomethyl)benzene dibromide, 1519-46-6; 4-pentynal, 18498-59-4

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[7] We thank Dr. *W. Brügel*, BASF, for recording these spectra.

Pentacarbonylmonosulfanetungsten, $W(CO)_5SH_2$[**]

By *Max Herberhold* and *Georg Süss*[*]

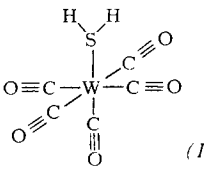
Although hydrogen sulfide reacts with many transition metal compounds, no stable transition metal complexes containing H_2S ligands have so far been reported. Evidently the initial products transform rapidly into complexes with SH ligands or polynuclear complexes with S bridges[1]. Apart from the very unstable "thiohydrates" of a few Lewis acids (*e.g.* $TiCl_4 \cdot xH_2S$, $TiBr_4 \cdot xH_2S$; x = 1, 2)[2] there is ^{1}H-NMR spectroscopic evidence of a platinum complex $(Ph_3P)_2Pt(SH_2)$, which, however, is already converted into the hydride $(Ph_3P)_2Pt(H)(SH)$ in solution[3]. A green manganese complex previously described as "$C_5H_5Mn(CO)_2SH_2$"[4a] has been shown to have the composition $[C_5H_5Mn(CO)_2]_2S$[4b] (cf. Ref. [10]).

We have found that photolysis of hexacarbonyltungsten in solution with simultaneous passage of H_2S gas leads to a relatively stable complex $W(CO)_5SH_2$ *(1)*:

$$W(CO)_6 + H_2S \xrightarrow[\text{n-Pentane}]{h\nu} W(CO)_5SH_2 + CO$$

(1)

The diamagnetic product *(1)* can be isolated from *n*-pentane as green lustrous crystals, which decompose at *ca.* 90 °C in a sealed tube under N_2; in solution (benzene, ether, acetone) the complex slowly decomposes at room temperature. In a high vacuum, *(1)* is volatile at 20 °C although it undergoes partial decomposition.



(1)

All spectroscopic findings indicate that *(1)* contains an unchanged H_2S ligand:

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[**] This work was supported by the Fonds der Chemischen Industrie. *G. S.* is indebted to the Studienstiftung des Deutschen Volkes for a postgraduate grant.

The mass spectrum[5] shows the molecular ion $W(CO)_5SH_2^+$ (*m/e* 358, referred to ^{184}W) with the expected W/S isotopic distribution, as well as all fragments of the series $W(CO)_nSH_2^+$ ($n=4$—0); a further series of the type $W(CO)_nS^+$ ($n=4$—0) can be attributed to loss of hydrogen from $W(CO)_4SH_2^+$ (or the fragments poorer in CO) and to subsequent CO eliminations.

The IR spectrum of *(1)* shows the characteristic pentacarbonyl band pattern (ν(C≡O) 2076(w), 1971(m), 1935(s), and 1916(sh) cm^{-1} in benzene). An S—H valence absorption is observed at 2560 cm^{-1} (KBr)[6].

In the ^1H-NMR spectrum[7] of the complex the singlet of the H_2S protons is shifted downfield compared to free H_2S ($\delta=0.60$ ppm for *(1)* against 0.20 ppm for free H_2S, in each case in [D_8]-toluene at −11 °C). The satellites expected to arise from ^{183}W-^1H spin-spin coupling could not be observed[8a]. A marked downfield shift of the H_2S proton signal of *(1)* occurs in [D_6]-acetone; in addition the chemical shift shows a linear temperature dependence, as is characteristic for intermolecular hydrogen bonds [$\delta=3.93$ (−8 °C), 4.39 (−33 °C), and 4.65 ppm (−60 °C); the corresponding signals of free H_2S appear at $\delta=1.39$, 1.47, and 1.65 ppm[8b]]. It can be concluded from the ^1H-NMR spectrum that the acidity of hydrogen sulfide increases through coordination to the complex fragment [$W(CO)_5$].

Experimental[9a]

Dry H_2S gas is passed through a solution of $W(CO)_6$ (0.35 g, 1 mmol) in *n*-pentane (150 ml), which at the same time is irradiated with a high-pressure mercury arc (Hanovia S-200W). After 3 h the cloudy reaction mixture is filtered through filter flocks and the green filtrate concentrated at −30 °C to a volume of 50 ml. $W(CO)_5SH_2$ *(1)* crystallizes out almost completely. The green crystals are washed several times with *n*-pentane and then dried at −10 °C in a high vacuum; yield 0.11 g (31 %)[9b].

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German version: Angew. Chem. *88*, 375 (1976)

CAS Registry numbers:
(1), 58802-43-0; $W(CO)_6$, 14040-11-0

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[5] Atlas CH4, ion source TO4; investigations by Dr. *F. Kreissl* and *W. Uedelhoven*.—The less stable chromium complex $Cr(CO)_5SH_2$ was also characterized mass spectroscopically.
[6] The fundamental vibrations of the H_2S molecule in the gaseous state were assigned as ν_1 2615 (A_1), ν_2 1183 (A_1), ν_3 2354 (B_1) cm^{-1}: cf. *H. C. Allen Jr., L. R. Blaine*, and *E. K. Plyler*, J. Chem. Phys. *24*, 35 (1956); *H. C. Allen Jr.* and *E. K. Plyler, ibid. 25*, 1132 (1956).
[7] Jeol C 60 HL; investigations by Dr. *C. G. Kreiter*.
[8] a) The ^{183}W-^1H coupling constant is presumably small; in the case of $W(CH_3)_6$ a value of 3.0 Hz was found for $^2J(^{183}W$-$^1H)$: *H. Shortland* and *G. Wilkinson*, J. C. S. Chem. Commun. *1972*, 318; J. C. S. Dalton *1973*, 872.—b) The sample contained complex *(1)* along with free H_2S; the temperature was determined from the signal splitting of methanol.
[9] a) All operations carried out under N_2.—b) A binuclear complex, $[W(CO)_4SH]_2$, (derived from *(1)*) can also be isolated.
[10] *Note added in proof:* The salts $[Ru(NH_3)_5SH_2](BF_4)_2$ (unstable) and *trans*-$[Ru(NH_3)_4(SH_2)(isn)](BF_4)_2$ (isn = isonicotinamide) have recently been described: *C. G. Kuehn* and *H. Taube*, J. Amer. Chem. Soc. *98*, 689 (1976).

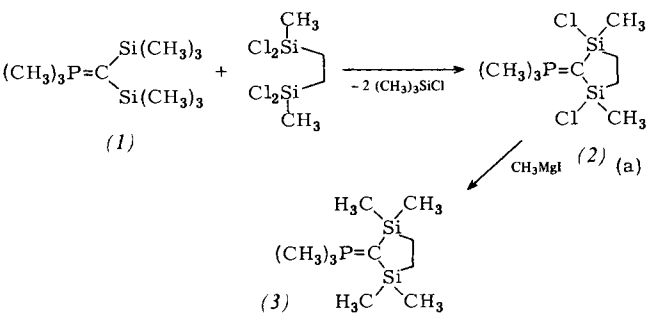
Base-Induced Intramolecular Cyclization of Silicon-Substituted Phosphorus Ylides

By *Hubert Schmidbaur* and *Michael Heimann*[*]

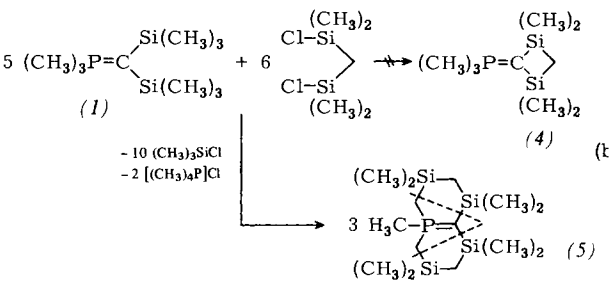
Incorporation of organosilicon substituents at the carbanion of phosphorus ylides can be carried out extraordinarily easily and leads to markedly stabilized products[1]. Transylidation or metalation steps frequently play a role, in which the acidification of protons α to the onium center of the ylide is exploited for synthetic purposes[2].

We have now found in investigations with difunctional organosilicon reagents that also cyclization at the carbanion of the ylide can be achieved, *viz.* by two transsilylation steps in accordance with Eq. (a). Should however the number of potential ring members be too small, then a completely different type of cyclization results if the acidic hydrogen atoms of the methyl groups on phosphorus are mobilized by ylide base or by metalation [Eqs. (b) and (c)].

Reaction of trimethylbis(trimethylsilyl)methylenephosphorane *(1)*[3] with 1,2-bis(methyldichlorosilyl)ethane leads, even at room temperature, in the sense of a transsilylation with loss of trimethylchlorosilane to the ylide heterocycle *(2)* in almost quantitative yield. Methylation of *(2)* with Grignard reagent affords the chlorine-free derivative *(3)*.



Reaction of *(1)* with bis(dimethylchlorosilyl)*methane*, on the other hand, leads to the bicyclic ylide *(5)*. The trans*silylation* proceeds in the molar ratio 1:2 with avoidance of the strained four-membered ring *(4)* (displacement of each of the two $(CH_3)_3Si$ groups of *(1)* by a disilylmethane)[4]. The excess of ylide finally deprotonates successively two of the three methyl groups on phosphorus, thus opening the way for cyclization at these functions and hence for the formation of *(5)*. The withdrawal of protons from alkyl groups of phosphonium centers by ylides is a trans*ylidation* step, which explains the formation of corresponding amounts of phosphonium salt (the broken line in formula *(5)* delineates the reaction components).



Closure of a single six-membered ring is possible by reaction of the same disilylmethane component with doubly lithiated trimethylmethylenephosphorane:

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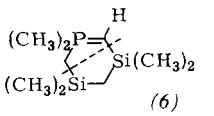
$$(CH_3)_3P{=}CH_2 \xrightarrow[-2\ RH]{+2\ LiR} CH_3P(CH_2)_3Li_2 \xrightarrow[-2\ LiCl]{+CH_2[Si(CH_3)_2Cl]_2} \quad (c)$$

(4) + 

(6)

Here, the metalation of the starting ylide corresponds to the deprotonation by excess ylide base. The remaining hydrogen atoms are redistributed in the end products by proton shifts so that the ylide function bears at least one carbanion-stabilizing silyl substituent[1].

In this way *(6)* is formed as the major component of a difficultly separable mixture, which also contains *(4)*. Although *(6)* can be isolated by fractional distillation, separation of completely pure *(4)* has so far not been achieved. If *(6)* is converted into its hydrochloride, however, pure *(4)* remains after filtration. The cyclic silyl ylides *(2)*—*(6)* are highly reactive and remarkably thermostable colorless compounds. Investigation of their chemical properties is in progress[5].

Experimental:

Monocycles (2) and *(3)*: A mixture of *(1)* (14.3 g, 61 mmol) and $[Cl_2(CH_3)SiCH_2]_2$ (31.6 g, 123 mmol) in diethyl ether (100 ml) is stirred for 15 h and then distilled at 25 °C: yield of *(3)* 14.8 g (89 %), b.p. 106—107 °C/0.1 torr.—To a solution of *(2)* (11.2 g) in ether is added dropwise a solution of 2 equivalents of CH_3MgI and the mixture stirred for 15 h at 20 °C; the precipitate is filtered off and the filtrate fractionated: yield of *(3)* 5.7 g (61 %), b.p. 42—45 °C/0.1 torr. ^{1}H-NMR (C_6H_6, TMS external): CH_3Si 0.13 (s, 12H), CH_2 0.87 (s, 4H), CH_3P 0.97 ppm (d, 9H; J(HCP) = 12 Hz).

Bicycle (5): A mixture of *(1)* (4.25 g, 18.1 mmol) and $[Cl(CH_3)_2Si]_2CH_2$ (4.38 g, 21.8 mmol) in the absence of solvent is heated for 48 h at 80 °C. Subsequent filtration and distillation affords 2.2 g (58 %) of *(2)*, b.p. 80 °C/0.1 torr, subl. 25—30 °C/0.001 torr; m.p. 58—59 °C, ^{1}H-NMR (C_6H_6, TMS ext.): CH_3Si −0.07 (s, 12H), 0.25 (s, 6H), 0.29 (s, 6H), CH_2Si −0.60 (s, 4H), CH_2P 0.27 (d, 4H; J(HCP) = 15 Hz), CH_3P 0.67 ppm (d, 3H; J(HCP) = 11.5 Hz). ^{13}C-NMR (in $C_6D_5CD_3$ against C^1, ΔTMS 137 ppm): CH_3Si 17.1 (s), 16.4 (s), 16.1 (s), CH_2Si 12.6 (s), CH_2P 30.9 (d; J(PC) = 44.1 Hz), CH_3P 37.9 ppm (d; J(CP) = 69.1 Hz). ^{29}Si-NMR (C_6D_6, TMS internal): −2.57 (d; J(SiCP) = 5.3 Hz), 3.91 ppm (d, J(SiCP) = 6.1 Hz). ^{31}P-NMR (C_6H_6, H_3PO_4 ext.): $\{^1H\}$ 6.17 ppm.

Monocycle (6): A solution of $(CH_3)_3P{=}CH_2$ (6.5 g, 72 mmol) in THF (40 ml) is treated with two equivalents of *n*-butyllithium in *n*-hexane at −10 °C. After 15 hours' stirring at 20 °C the reaction mixture is diluted with 600 ml THF, cooled to −20 °C, and then treated dropwise within a period of 5 h with a solution of $[Cl(CH_3)_2Si]_2CH_2$ (14.8 g, 73.5 mmol) in THF (100 ml). The solution is allowed to stand for a week at −18 °C; the solvent is removed in a vacuum and the residue filtered free of LiCl and then fractionated. Yield of *(6)* with *(4)*: 8.5 g (54 %), b.p. 100—120 °C or 30 °C/0.001 torr. *(6)* can be gradually enriched in the residue and finally isolated: b.p. 128 °C/50 torr. ^{1}H-NMR (C_6H_6, TMS ext.): CH_3Si −0.28 (d, 6H), −0.12 (d, 6H), CH_2Si −0.62 (s, 2H), CH_2P 0.01 (d, 2H; J(HCP) = 15 Hz), CH −0.89 (d, 1H; J(HCP) = 7.5 Hz), CH_3P 0.62 ppm (d, 6H; J(HCP) = 12.4 Hz). $\{^{31}P\}$-experiments confirmed the assignment of the signals to one and the same compound. After addition of an equivalent of ethereal HCl to bind all *(6)* contained in the mixture, filtration, and evaporation of solvent, pure *(4)* remains [b.p. 65 °C/2 torr, m.p. 23 °C; ^{13}C-$\{^1H\}$-NMR (C_6H_6): CH_3Si 7.3 (s), CH_2 2.9 (d, J(CSiCP) = 37 Hz), CH_3P 20.4 (d, J(PC) = 59 Hz). >C = 13.2 (d, J(PC) = 95 Hz).

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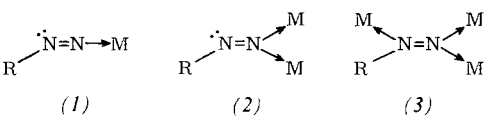
CAS Registry numbers:
(1), 3607-03-2; *(2)*, 58802-31-6; *(3)*, 58802-32-7; *(4)*, 58802-33-8; *(5)*, 58802-34-9; *(6)*, 58802-35-0; $[Cl_2(CH_3)SiCH_2]_2$, 3353-69-3; $[Cl(CH_3)_2Si]_2CH_2$, 5357-38-0; $(CH_3)_3P{=}CH_2$, 14580-91-7; ^{13}C, 14762-74-4; ^{29}Si, 14304-87-1; ^{31}P, 7723-14-0

[1] *H. Schmidbaur*, Acc. Chem. Res. *8*, 62 (1975).
[2] *N. E. Miller*, J. Am. Chem. Soc. *87*, 390 (1965); *H. Schmidbaur* and *W. Tronich*, Chem. Ber. *100*, 1032 (1967); *H. Schmidbaur* and *W. Malisch*, *ibid. 102*, 83 (1969); *103*, 97, 3448 (1970).
[3] *H. Schmidbaur* and *W. Tronich*, Chem. Ber. *100*, 1032 (1967); *N. E. Miller*, Inorg. Chem. *4*, 1458 (1965).
[4] *H. Schmidbaur* and *W. Malisch*, Chem. Ber. *104*, 150 (1971).
[5] We thank Hoechst AG (Werk Knapsack) and Wackerchemie (Burghausen) for generously supplying chemicals, the Fonds der Chemischen Industrie and the NATO Scientific Affairs Division (Brussels) for financial support, and Prof. *G. P. Van der Kelen* and Dr. *F. H. Köhler* for recording the ^{29}Si- and ^{13}C-NMR spectra, respectively.

μ-Methanediazo-(*N*,*N*,*N*′)-tris(tetracarbonylmanganese)[1]

By *W. A. Herrmann*, *M. L. Ziegler*, and *Klaus Weidenhammer*[*]

Structural interest and relevance to problems in nitrogen fixation by transition metal complexes have induced the present phase of intense investigation into arenediazometal derivatives[2]. To date, more than one hundred R—N=N complexes have been prepared which contain end-on coordinated ligands, as in *(1)* or *(2)*. The bridged structure *(2)* is represented by only one example[3]. In both coordination modes the *C*-bonded nitrogen atom possesses a free electron pair which should also be accessible to coordination. With the synthesis of methanediazo-(*N*,*N*,*N*′)-tris(tetracarbonylmanganese), $CH_3N_2[Mn(CO)_4]_3$, we have realized this structural possibility *(3)* for the first time.



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

The novel complex is formed in *ca.* 10 % yield among other products[4, 5] in the low temperature reaction of pentacarbonylmanganese hydride with diazomethane. Its composition was established as $C_{13}H_3Mn_3N_2O_{12}$ by total analysis, osmometric molecular weight determination, and high resolution mass spectrum. The latter exhibits the parent ion at m/e = 543.7796 as well as successive loss of all twelve carbonyl groups; the remaining carbonyl-free fragment $(Mn_3N_2CH_3)^+$ (m/e = 207.8439) undergoes an unusual fragmentation introduced by synchronous loss of Mn, HCN, and 2H. Because the analytical and spectroscopic data (Table 1) did not allow an unambiguous structure assignment we carried out a complete three dimensional X-ray analysis[6].

For the methanediazo complex the following structural characteristics were resolved (cf. Fig. 1):

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Table 1. Properties and crystal data of $CH_3N_2[Mn(CO)_4]_3$.

Deep red crystals; air-stable as a solid and in solution (diethyl ether, methylene chloride, acetone); dec. *ca.* 137°C	
IR: ν_{CO}:	2096 vw, 2056 vs (2051 m, sh), 2012 vs, 2002 m, 1988 w, 1970 m, 1964 m, and 1945 cm^{-1} vw (*n*-hexane)
$\nu_{N=N}$:	1586 cm^{-1} vw (KBr)
^{1}H-NMR:	$\tau CH_3 = 5.30$ ppm ([D$_6$]-acetone; TMS int. ref.)
Crystal data:	monoclinic (from Et_2O/CH_2Cl_2 1:1; −35°C) with $a = 989.1(2)$, $b = 1460.7(3)$, $c = 1319.6(5)$ pm, $\beta = 96.23(5)°$, $Z = 4$, $R = 4.5\,\%$, space group C_s^4

1) The metal carbonyl system consists of a bent Mn—Mn—Mn skeleton with typical metal-metal single bond distances.

2) The terminal diazo nitrogen N(1) forms a coordination bridge between Mn(2) and Mn(3), which forces the central manganese atom Mn(2) to have the unusual coordination number 7. According to the noble gas configuration of the metal centers, N(1) formally has to act as a *one*-electron donor towards Mn(2) and as a *two*-electron donor towards Mn(3). The N(1)—Mn(2) and N(1)—Mn(3) distances therefore differ.

3) Acting as a two-electron donor, the central nitrogen atom is bonded to only *one* tetracarbonylmanganese fragment. The N(2)—Mn(1) bond is significantly longer than both the remaining manganese-nitrogen bonds and is hardly likely to contain extensive back bonding contributions.

4) The entire Mn_3N_2C-unit lies within ±1.96 pm of the molecular plane. Mn(1) and Mn(3) have distorted octahedral environment, whereas Mn(2) is at the center of a distorted pentagonal bipyramid.

5) The nitrogen-nitrogen bonding distance (122.4 pm) corresponds to a typical double bond. The metal coordination of N(2) seems to have no effect upon this bond length, but causes a considerable reduction of the NNC angle from 119.7° in the comparable compound $[(CO)_4Mn—N=N—C_6H_5]_2$[3] to 112.3° in the molecule discussed here.

Distances [pm]:		Angles [°]:	
Mn(1)—Mn(2)	282.6(3)	Mn(1)—Mn(2)—Mn(3)	107.4(7)
Mn(2)—Mn(3)	280.7(4)	N(2)— N(1) —Mn(2)	119.9(7)
N(1)—Mn(2)	196.4(8)	Mn(2)— N(1) —Mn(3)	93.8(4)
N(1)—Mn(3)	187.9(8)	N(2)— N(1) —Mn(3)	146.2(7)
N(2)—Mn(1)	206.1(8)	Mn(1)— N(2) —N(1)	107.2(6)
N(1)—N(2)	122.4(11)	N(1)— N(2) —C(1)	112.3(12)
N(2)—C(1)	156.9(15)	Mn(1)— N(2) —C(1)	140.5(11)

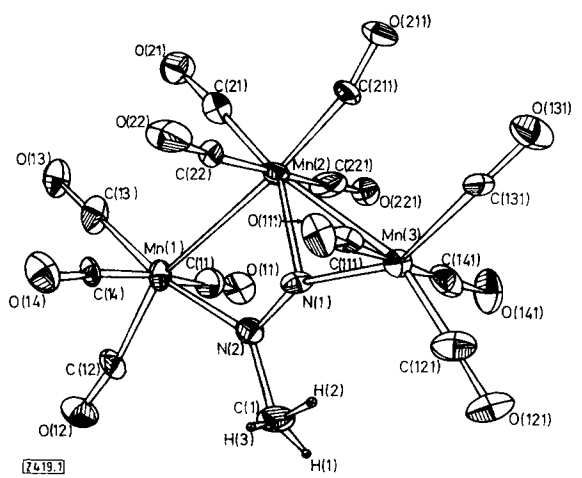

Fig. 1. ORTEP plot of $CH_3N_2[Mn(CO)_4]_3$. The thermal ellipsoids have 50% probability; all atoms are drawn in proper dimensions except hydrogen.

The overall geometry of an end-on complexed R—M=N moiety is not affected in its essential parameters by additional N(2) coordination. According to our results, the introduction of neutral metal carbonyl protecting groups into complexes of the types *(1)* and *(2)* for performing chemical reactions in other parts of the molecule seems promising. Moreover, the preparation of $CH_3N_2[Mn(CO)_4]_3$ shows the utility of diazomethane for the synthesis of the hitherto poorly studied *alkane*diazo compounds[2, 7].

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CAS Registry number:
$CH_3N_2[Mn(CO)_4]_3$, 58832-58-9

[1] Complex Chemistry of Reactive Organic Compounds, Part 13.—Part 12: *W. A. Herrmann*, Chem. Ber., in press.
[2] *D. Sutton*, Chem. Soc. Rev. *4*, 443 (1975).
[3] *E. W. Abel, C. A. Burton, M. R. Churchill*, and *K.-K. G. Lin*, J. C. S. Chem. Commun. *1974*, 268.
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[5] A comprehensive description of the reaction systems $CH_2N_2/(CO)_5MH$ (M = Mn, Re) is found in: *W. A. Herrmann, H. Biersack, K. K. Mayer*, and *R. D. Minard*, Chem. Ber., in press.
[6] 1647 independent non-zero reflections were recorded with an automatic Siemens single crystal diffractometer (Mo-K_α irradiation) and corrected in the usual manner (*M. L. Ziegler* and *K. Weidenhammer*, to be published).
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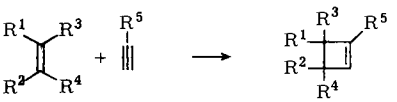
[2+2]-Cycloaddition of Alkynes to Alkenes[**]

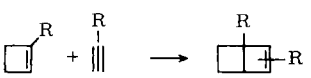
By *Joachim H. Lukas, Frank Baardman*, and *Arjan P. Kouwenhoven*[*]

[2+2] Cycloadditions of allenes to alkenes are feasible in the presence of Lewis acid catalysts[1]. We suspect the reaction to involve a complex of the allene with the Lewis acid which is polarized in the direction of a vinyl cation.



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

We have now found that under similar reaction conditions the allene can be replaced by a 1-alkyne *(2)*; reaction with alkenes *(1)* then affords cyclobutenes *(3)* (Table 1). Dialkyl-substituted alkynes give polymeric products or trimerize to hexaalkyl-benzenes or -Dewar benzenes. Trimerization to 1,3,5-trialkylbenzene occurs as a side reaction with 1-alkynes. In general the ratio of trialkylbenzene to cyclobutene decreases as the size of the alkyl group in the alkyne increases[2].



R = Alkyl *(4)*

Table 1. Examples of [2+2] cycloaddition of 1-alkynes *(2)* to alkenes *(1)* affording cyclobutenes *(3)*.

Cpd.	R^1	R^2	R^3	R^4	R^5	Yield [%]
cis-(3a)	CH_3	CH_3	H	H	C_2H_5	5
(3b)	CH_3	CH_3	CH_3	CH_3	CH_3	27
(3c)	CH_3	CH_3	CH_3	CH_3	C_2H_5	35
(3d)	CH_3	CH_3	CH_3	CH_3	C_3H_7	50
(3e)	CH_3	CH_3	CH_3	CH_3	$CH_2CH(CH_3)_2$	60
(3f)	CH_3	CH_3	CH_3	CH_3	C_5H_{11}	50
(3g)	—CH_2—CH=CH—CH_2—		H	H	C_2H_5	40
(3h)	H	CH_3	H	CH_3	C_2H_5	30

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[**] [2+2] Cycloadditions, Part 2.—Part 1: ref. [1].

Further cycloadditions occurring as secondary reactions lead to bicyclo[2.2.0]hexenes *(4)*. The position of the alkyl group on the double bond of *(4)* is not yet known.

1,3,3,4,4-Pentamethyl-1-cyclobutene (3b)

2,3-Dimethyl-2-butene (2.5 g) and a 4 M solution of ethylaluminum dichloride (0.5 ml) in *n*-hexane are successively added to chlorobenzene (20 ml) saturated with propyne, a stream of propyne being passed through the mixture for the duration of the reaction. An exothermic reaction is accompanied by red to brown coloration. As soon as the dimethylbutene has disappeared from the solution (GLC) it is shaken with water to destroy the catalyst and dried over magnesium sulfate. Compound *(3b)* is isolated by fractional distillation; b.p. 116 °C, yield 1.0 g (27 %).

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CAS Registry numbers:
(1a), 107-01-7; *(1b)*, 563-79-1; *(1g)*, 628-41-1; *(1h)*, 115-11-7; *(2a)*, 107-00-6; *(2b)*, 74-99-7; *(2d)*, 627-19-0; *(2e)*, 7154-75-8; *(2f)*, 628-71-7; *cis-(3a)*, 58784-36-4; *(3b)*, 54562-59-3; *(3c)*, 54562-60-6; *(3d)*, 54562-61-7; *(3e)*, 54562-62-8; *(3f)*, 54562-63-9; *(3g)*, 54562-65-1; *(3h)*, 58784-37-5

[1] *J. H. Lukas, A. P. Kouwenhoven*, and *F. Baardman*, Angew. Chem. *87*, 740 (1975); Angew. Chem. Int. Ed. Engl. *14*, 709 (1975).
[2] [2+2] Cyclodi- and -trimerizations of alkynes under the influence of acids are known; see [1], references [2, 3, 5].

A New Electrochemical Method of Forming SiSi Bonds

By *Edwin Hengge* and *Georg Litscher*[*]

Only few methods are presently available for generating SiSi linkages. The most commonly used approach in preparative applications consists in a Wurtz-type reaction of halosilanes with an alkali metal. Variants of this reaction, *e.g.* coupling of a halosilane with an organometallic silicon derivative, can be utilized if the corresponding reagents are accessible. Nonspecific methods include pyrolysis and degradations of polymeric structures (*e.g.* of silicides). In isolated cases the photolysis of mercury compounds and dehydrogenation of Si—H bonds with di-*tert*-butyl peroxide may be successful[1].

We have now developed a method whereby products having new SiSi bonds can be obtained under extremely mild conditions from halosilanes. Electrolysis of, *e.g.*, trimethylchlorosilane (Me_3SiCl) in 1,2-dimethoxyethane in the presence of a supporting electrolyte, *e.g.* $[(n\text{-}Bu)_4N]ClO_4$, with mercury electrodes yields hexamethyldisilane ($Me_3SiSiMe_3$). Any aprotic solvent can be used provided that it is stable under the reaction conditions, *e.g.* tetrahydrofuran. Apart from quaternary ammonium salts, lithium chloride can also be used as supporting electrolyte. Desirable, but not essential, is the use of a diaphragm (glass frit).

Of great importance is the choice of electrodes. Lead and mercury have proved suitable as cathode material, lead having the advantage of being a solid and thus favoring a more convenient cell geometry. Apart from lead and mercury, graphite is also suitable as anode material. $PbCl_2$ and Hg_2Cl_2 are formed on use of lead and mercury, respectively. In the case of mercury it suffices to vigorously stir the surface of the electrode to counteract passivation of the electrodes by the chloride. Passivation is also observed with graphite anodes. Platinum is rather susceptible to corrosion when used as anode material. The most suitable cell employed so far has a lead cathode and a mercury anode.

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The electrochemical synthesis of hexamethyldisilane from trimethylchlorosilane will now be considered as a typical procedure illustrating the new method for generating SiSi linkages. The sensitivity of the halosilanes to hydrolysis requires rigorous exclusion of moisture; dry oxygen-free nitrogen is used as inert gas. Electrolysis is performed in a glass vessel with a mercury pool as anode and a lead cathode (current supply by platinum wire sealed into glass); the electrode cross section is 40 cm^2 and the distance between the electrodes is 1.5 cm. Stirring is accomplished with a magnet floating on the mercury. A 150-ml quantity of electrolyte solution—composition 60% 1,2-dimethoxyethane, 40% trimethylchlorosilane, 1 g (0.02 mol/l) of $[(n\text{-}Bu)_4N]ClO_4$—electrolyzed at room temperature, 75 V potential difference, and 1 mA/cm^2 current density afforded hexamethyldisilane in *ca.* 95 % current efficiency. The product isolated by distillation and identified by its boiling point and Raman spectrum is free from hexamethyldisiloxane. The product yield clearly depends upon the duration of electrolysis, *e.g.* 10 g of $Me_3SiSiMe_3$ was obtained after 4 days.

The method appears to have a wide scope. Triphenylchlorosilane can be transformed into hexaphenyldisilane; but also difunctional compounds such as diphenyldichlorosilane react to give hitherto uncharacterized oligomers and polymers (nondistillable oils). Since the use of separate electrode compartments permits contact between substrate and electrode material only and, in contrast to the "Wurtz reaction", the method can be used at low temperatures, it also appears suitable for complicated and sensitive halosilanes.

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German version: Angew. Chem. *88*, 414 (1976)

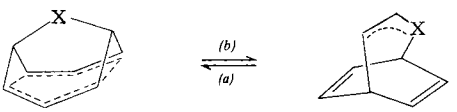
CAS Registry numbers:
$Me_3SiSiMe_3$, 1450-14-2; trimethylchlorosilane, 75-77-4

[1] Review: *E. Hengge*, Fortschr. Chem. Forsch. *51*, 1 (1974).

Unsubstituted 9-Azabarbaralane; A π-Destabilized Heterocycle[**]

By *A. G. Anastassiou, E. Reichmanis*, and *A. E. Winston*[*]

Recent experimental work with 9-barbaralyl ions *(1a)*[1] and *(1b)*[2] has demonstrated that p-orbital occupancy at C-9 exerts decisive control on their overall stability. Specifically, ion *(1)* was found to readily interconvert with tautomer *(2)* by a process which is strictly charge controlled and whose direction reveals *(1)* to be π-stabilized as the cation *(1a)* and π-destabilized as the anion *(1b)*.



(1) *(2)*

(a), X = $\overset{\oplus}{C}H$; *(b)*, X = $\overset{\ominus}{C}H$

In light of the above findings we resolved to prepare and examine parent 9-azabarbaralane *(7)* for possible signs of lone-pair induced destabilization.

The steps employed in the synthesis of unsubstituted 9-azabarbaralane *(7)*[3] and its *N*-methyl derivative *(8)*[3] from known[4] azabicyclotrienes *(3)* and *(4)* are given below. Based

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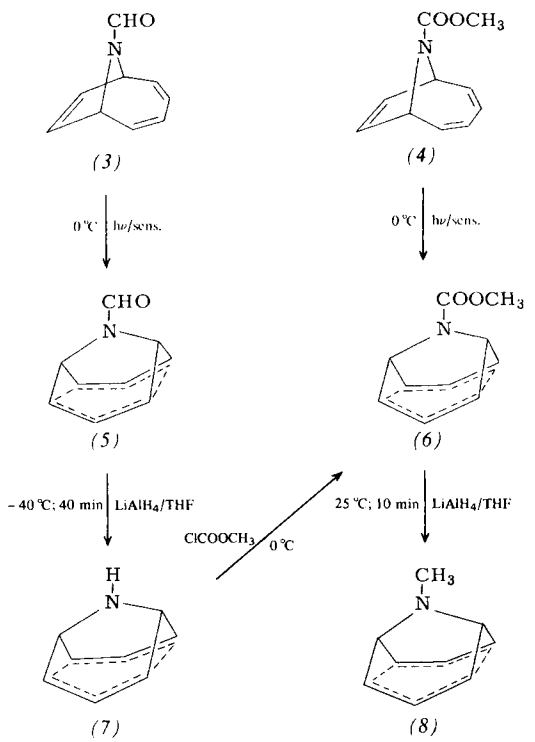
on their response to thermal excitation the azabarbaralanes described here are divisible into two distinct categories: the pair *(7)* and *(8)* readily rearranges at ambient temperature[5] whereas *(5)*[3,6,7] and *(6)*[3,7] effectively resist change even at elevated temperatures. The difference between the two classes is perhaps best exemplified by direct comparison between *(7)* whose half-life was found (NMR; [D_6]-acetone) to be a mere 18 min ($\Delta G^{\neq} \approx 22$ kcal/mol) at 32 °C and *(5)* which may be recovered unchanged (NMR) after being heated at 140 °C for 30 min! Since of the four 9-azabarbaralanes described here the two that are thermally unstable, *viz. (7)* and *(8)*, are also the only members that incorporate lone pairs which are well accessible electronically for interaction with the homotropilidine moiety of the molecule, one must conclude that the nitrogen lone pair exerts a destabilizing effect on the 9-azabarbaralane system.



Significantly, the notion that lone-pair participation leads to skeletal destabilization of the 9-heterobarbaralane frame receives added support from the observation that the thermal stability of parent amine *(7)* in [D_6]-acetone increases substantially in strongly acidic media, the amount of rearrangement (NMR) decreasing from 50% in 18 min at 32 °C (see above) to <10% in 18 h at 35 °C upon addition of a drop of trifluoroacetic acid.

The situation described here for the 9-azabarbaralanes sharply contrasts with that found in the isomeric azonines where the lone pair exerts a stabilizing influence on the π system[8] but is reminiscent of that encountered with the azepine family where the π system is known to effectively reject the nitrogen lone pair[9]. In short, the unsubstituted fluctional 9-azabarbaralane system shows clear signs of antiheteroaromatic character.

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CAS Registry numbers:
(3), 35105-37-4; *(4)*, 38114-09-9; *(5)*, 58832-20-5; *(6)*, 58832-21-6; *(7)*, 58832-22-7; *(8)*, 58832-23-8

[1] *P. Ahlberg, D. L. Harris,* and *S. Winstein*, J. Am. Chem. Soc. *92*, 4454 (1970).
[2] *M. J. Goldstein, S. Tomoda, S. I. Murahashi, K. Hino,* and *I. Moritani*, J. Am. Chem. Soc. *97*, 3847 (1975).
[3] This substance was characterized by fully consistent spectroscopic (NMR, IR, UV, MS) data.
[4] *A. G. Anastassiou* and *R. P. Cellura*, J. Org. Chem. *37*, 3126 (1972).
[5] Thus far, several attempts at characterizing the thermolysis product(s) by isolation or trapping have proven unsuccessful.
[6] The ^{1}H-NMR spectrum taken at ambient temperature shows distinct signs of molecular asymmetry due to restricted rotation of the *N*-substituent.
[7] The elemental composition of this substance was established by C,H,N combustion analysis.
[8] The subject was recently reviewed: *A. G. Anastassiou*, Acc. Chem. Res. *5*, 281 (1972); *A. G. Anastassiou* in *T. Nozoe, R. Breslow, K. Hafner, S. Ito,* and *I. Murata:* Topics in Nonbenzenoid Aromatic Chemistry. Vol. 1. Hirokawa Publishing Co., Tokyo 1973, pp. 1–27.
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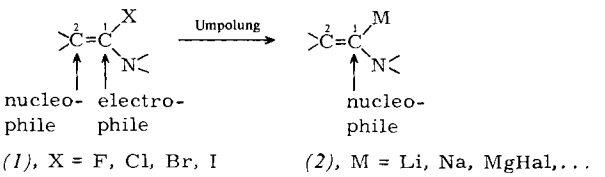
α-Metalated Enamines[**]

By *Chantal Wiaux-Zamar, Jean-Paul Dejonghe, Léon Ghosez, J. F. Normant,* and *J. Villieras*[*]

α-Haloenamines *(1)*[1] react as electrophiles at C-1 and as nucleophiles at C-2. In principle, umpolung of C-1 could be achieved by replacing the carbon-halogen bond by a carbon-



(1), X = F, Cl, Br, I *(2)*, M = Li, Na, MgHal, ...

metal bond. The resulting organometallic compounds *(2)* should behave as synthetic equivalents of acyl anions[2].

In order to establish the reactions of *(2)*, the thermally stable α-chloroenamines *(1a)*–*(1c)* were treated with metallic reagents and then with D_2O (Table 1). The resulting mixtures were analyzed by GLPC and NMR. In independent experiments, products *(3)* and *(4)* were separated and purified and their structures were established by spectroscopic methods or by comparison with authentic samples. The dienes *(4a)*

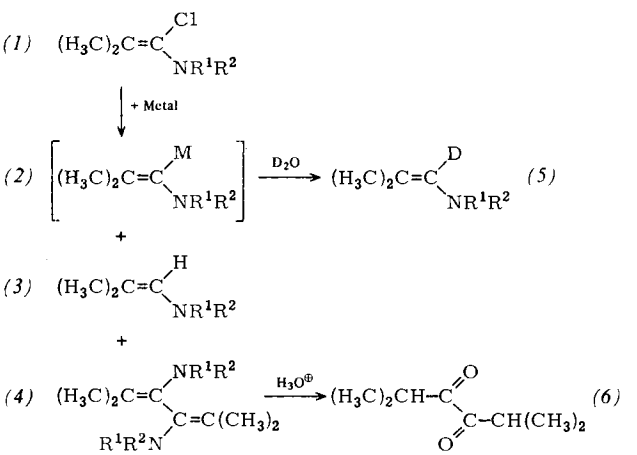


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Table 1. Reactions of α-chloroenamines *(1)* with metals *via* the organometallic compounds *(2)* to form the enamines *(3)* and/or *(4)* and/or *(5)*. In all cases, the concentration of *(1)* was ≈0.25 mol/l.

(1)	R^1	R^2	M	Solvent	T[°C]	(2) [a]	Yield [%] (3)	(4)	(5)
(1a)	$-(CH_2)_2-O-(CH_2)_2-$		Li	Ether	Reflux	—	0	0	0
(1a)	$-(CH_2)_2-O-(CH_2)_2-$		Li	THF	50—60	—	30	40	0
(1a)	$-(CH_2)_2-O-(CH_2)_2-$		Na	THF	20	—	79	9	4.3
(1a)	$-(CH_2)_2-O-(CH_2)_2-$		Na	Hexane	20	—	54	29	10
(1a)	$-(CH_2)_2-O-(CH_2)_2-$		Mg	Ether	Reflux	—	0	0	0
(1a)	$-(CH_2)_2-O-(CH_2)_2-$		Mg	THF	40—45	30	33	12	33
(1b)	CH_3	CH_3	Mg	THF	60	0	0	50	0
(1c)	CH_3	C_6H_5	Mg	THF	40—50	79	30	0	70

[a] Determined by titration with 2,2'-biquinoline [3].

and *(4b)* were readily hydrolyzed to give the α-diketone *(6)*.

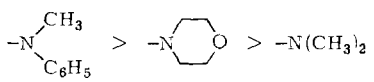
The following observations can be made on the basis of Table 1:

1) Metal-chlorine exchange only occurs in a basic solvent such as tetrahydrofuran (except for Na).

2) The formation of α-metalated enamines *(2)* has been unequivocally demonstrated either by titration or by deuterolysis.

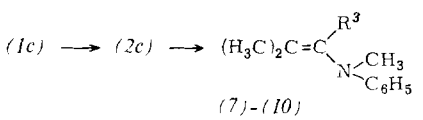
3) Products *(3)* and *(4)* were already present in the mixture before deuterolysis.

4) The amine substituent in *(1)* determines the yield of *(2)* as shown:



This is the reverse order of that observed for the ionization of *(1)* to keteniminium chlorides[1].

The potential of α-metalated enamines *(2)* for nucleophilic aminoalkenylation[4] is illustrated in Table 2 for the case of *(2c)*. It is not yet known to what extent the alkenyl group can be varied.



(7)-(10)

Table 2. Nucleophilic aminoalkenylation with *(2c)*. The yields are based on *(1c)*.

Cpd.	R^3	Reagents	Yield [%] M.p. [°C] or b.p. [°C/torr] [b]
(7) [a]	COOH	1) CO_2	70
		2) $H_3O^{\oplus}$	142
(8)	$CH(CH_3)OH$	1) CH_3CHO	53
		2) NH_4Cl	$80/5 \times 10^{-3}$
(9)	$CO-CH_3$	1) $(CH_3CO)_2O$	59
		2) NH_4Cl	$70/10^{-2}$
(10)	$(H_3C)_2N-C=C(CH_3)_2$	1) *(1b)*	69
		2) NH_4Cl	88/0.1

[a] Compound *(7)* exists as a zwitterion.
[b] Pot temperature (bulb to bulb distillation).

The structures of the new products *(7)*, *(8)*, *(9)*, and *(10)* were proved by IR, ^{1}H-NMR, and mass spectra. No reaction occurred when *(2c)* was exposed to ethyl acetate or acetonitrile.

4-Methyl-3-(N-methylanilino)-3-penten-2-one (9)

Magnesium (0.549 g, 0.02 mol) covered with dry THF (5 ml) containing *(1c)* (20 drops) and a crystal of iodine were slowly warmed with stirring to about 40°C. Then the remaining *(1c)* (total amount: 1.657 g ≙ 0.008 mol) in THF (30 ml) was slowly added to the colorless solution at 40°C. After addition was complete, the mixture was stirred for two hours at 40—50°C. All the operations were performed under an argon atmosphere. The THF solution of the Grignard reagent was then added from a syringe to acetic anhydride (0.879 g, 0.008 mol) in THF (2 ml) cooled at −60°C. The mixture was hydrolyzed with an aqueous solution of NH_4Cl and extracted with CH_2Cl_2. The organic phase was worked up with 10% aqueous $NaHCO_3$, dried, and concentrated. The residue (1.677 g) was shown by NMR to contain 72% of *(9)* and 28% of *(3c)*. Bulb to bulb distillation gave pure *(9)* (1.036 g, 59%).

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(1a), 58933-80-5; *(1b)*, 26189-59-3; *(1c)*, 58933-81-6; *(2a)*, 58933-82-7; *(2c)*, 58933-83-8; *(3a)*, 2403-55-6; *(3c)*, 25076-84-0; *(4a)*, 58933-84-9; *(4b)*, 58933-85-0; *(5a)*, 58933-86-1; *(5c)*, 58933-87-2; *(6)*, 4388-87-8; *(7)*, 58933-88-3; *(8)*, 58933-89-4; *(9)*, 58933-90-7; *(10)*, 58933-91-8

[1] *L. Ghosez* and *J. Marchand-Brynaert*, Adv. Org. Chem. *9* (1976), in press.
[2] *U. Schöllkopf* and *P. Hänssle*, Justus Liebigs Ann. Chem. *763*, 208 (1972); *J. E. Baldwin, G. A. Höffe*, and *O. W. Lever Jr.*, J. Am. Chem. Soc. *96*, 7125 (1974); *J. Hartmann, M. Stähle*, and *M. Schlosser*, Synthesis *1974*, 888, and references cited therein.
[3] *S. E. Watson* and *J. F. Eastham*, J. Organomet. Chem. *9*, 165 (1967).
[4] For electrophilic aminoalkylation, see *J. Marchand-Brynaert* and *L. Ghosez*, J. Am. Chem. Soc. *94*, 2869 (1972).

1,3,2-Dioxazolidines by Thermal 1,3-Cycloaddition of Nitro Groups to Strained Olefins

By *Johannes Leitich*[*]

Whereas nitro groups (in the $n\pi^*$ triplet state) are known to undergo photochemical 1,3-addition to olefins, forming 1,3,2-dioxazolidines[1], the corresponding thermal reaction—a "1,3-dipolar cycloaddition"[2] of the nitro group in the electronic ground state—has not been observed so far[2, 3].

We have found this thermal 1,3-cycloaddition to take place when the olefin component is highly strained[4], such as (*Z,E*)-1,5-cyclooctadiene *(2)*, and the nitro component is a nitrobenzene bearing additional electron-withdrawing groups, such as *(1)*. At room temperature (RT) *(1)* and *(2)* smoothly form the adducts *(3a)* to *(3d)* within one to several days.

The reactions proceed at the same rates in the dark or in daylight and at similar rates in various solvents. The steric course is uniform: catalytic hydrogenation of the crude reac-

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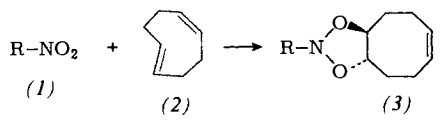

(1) *(2)* *(3)*

(a), R = 4-NC-C_6H_4
(b), R = 4-O_2N-C_6H_4
(c), R = 3-O_2N-C_6H_4
(d), R = 3-O_2N-5-H_3COOC-C_6H_3
(e), R = C_6H_5

tion mixture from *(1b)* and *(2)* affords *trans*-1,2-cyclooctanediol together with less than 0.3% of the *cis* isomer (GC).

The structure of the adducts *(3)* follows from their CHNO analysis, molar mass, IR and ^{1}H-NMR spectra[1], and especially from the partial hydrogenation of *(3b)* in ethyl acetate with Pd/C, which yields (*Z*)-5-cyclooctene-*trans*-1,2-diol and 4-nitroaniline.

Formation of the adduct *(3e)* from unsubstituted nitrobenzene *(1e)* and *(2)* can just compete with the dimerization of *(2)*[5] (NMR), while no adduct is formed at all with 1-methoxy-4-nitrobenzene or CD_3NO_2 (as solvent) and *(2)*.

The bimolecular rates of formation (l mol^{-1} s^{-1} × 10^6; acetonitrile, 25 °C) of *(3b)* (82) and *(3a)* (7.3) [compared with that of *(3e)* (0.65)] lead on Hammett correlation with the σ_p values[6] to a similar ρ value (2.2) as is obtained for *(3c)* (43) and *(3d)* (150) with the σ_m values (2.4); in contrast, the σ_p^- values afford 1.4. This shows that the electron deficiency at the reacting nitro group is mainly responsible for the addition rather than resonance between the nitrogen lone pair set free during the addition and a (−M) substituent on the benzene ring. Compound *(1b)* reacts about 400 times more slowly with (*E*)-cyclooctene than with *(2)*, corresponding to a difference of 3.5 kcal/mol in $\Delta G^{\neq}$. This accounts for only a small portion of the difference in heats of reaction of *ca.* 12 kcal/mol[4], from which it is deduced that the addition transition state must resemble the starting compounds more closely than the adduct.

The adducts *(3)* are stable for several days in aprotic solvents at room temperature, but rapidly decompose in protic media (methanol). Crystalline *(3a)* and *(3b)* can be stored indefinitely at room temperature. Hence the electron-withdrawing substituents both accelerate the addition and stabilize the adduct.

2-(p-Nitrophenyl)-3a,9a-trans-6,7-cis-3a,4,5,8,9,9a-hexahydrocycloocta[c][1,3,2]dioxazole (3b)[7]

Compounds *(2)* (1 g) and *(1b)* (1.55 g) are left to stand for 2 days at room temperature in tetrahydrofuran (18 ml). The pale yellow solution turns orange. Removal of the solvent at room temperature, addition of chloroform (10 ml) to the residue (dissolution is incomplete), addition of pentane (10 ml), cooling to −70 °C, reheating to room temperature, and rapid filtration under suction afford 0.12 g of unchanged *(1b)*. Treatment of the mother liquor by addition of pentane (40 ml), crystallization at −70 °C, and filtration under suction in the cold yields 1.64 g of crude *(3b)* [containing 7 wt % of *(1b)*]. It is dissolved in warm pentane, freed from small amounts of amorphous orange solids by filtration, and recrystallized at −70 °C. Remaining *(1b)* is sublimed off from the crystals at 50 °C/0.1 torr. Renewed dissolution in pentane, filtration, and crystallization affords pure *(3b)* as yellowish-white crystals, m.p. 101 °C (dec.); UV spectrum (*n*-hexane), λ_{max} = 306 nm (ε = 8900); ^{1}H-NMR ($CDCl_3$, TMS): δ = 1.1–1.9 (m, 2H), 2.0–2.5 (m, 6H), 4.2 (br. AA′ in AA′XX′ system, 2H), 5.65 (m, 2H), 7.45 and 8.2 ppm (AA′BB′ system, 4H). Decomposition occurs on the usual chromatographic adsorbents.

In similar manner *(2)* (1 g) and *(1a)* (2.37 g) in tetrahydrofuran (20 ml) afford, on standing for 5 days, 1.25 g of crude *(3a)* [containing 18 wt % of *(1a)*]. Analogous workup yields pure *(3a)*, colorless crystals, m.p. 98 °C (dec.); UV spectrum (*n*-hexane), λ_{max} = 266 nm (ε = 13200).

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(1a), 619-72-7; *(1b)*, 100-25-4; *(1c)*, 99-65-0; *(1d)*, 2702-58-1; *(1e)*, 98-95-3; *(2)*, 5259-71-2; *(3a)*, 58919-56-5; *(3b)*, 58919-57-6; *(3c)*, 58919-58-7; *(3d)*, 58919-59-8; *(3e)*, 58919-60-1

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[2] *R. Huisgen,* Angew. Chem. *75*, 604 (1963); Angew. Chem. Int. Ed. Engl. *2*, 565 (1963).
[3] Intramolecular 1,3-dipolar addition of a nitro group to another 1,3-dipole, see *R. Grashey,* Angew. Chem. *74*, 155 (1962); Angew. Chem. Int. Ed. Engl. *1*, 158 (1962).
[4] A measure for the "addition strain" can be seen in the difference Δ between the heats of reaction of the following Diels-Alder additions: cyclopentadiene + C=C double bond in question and cyclopentadiene + unstrained double bond in (*E*)-2-butene. The value of Δ is −17.5 and −5.6 kcal/mol respectively for *(2)* and (*E*)-cyclooctene (*E. Koch, B. Stilkerieg,* and *J. Leitich,* unpublished experiments). Cf. also: *R. B. Turner, B. J. Mallon, M. Tichy, W. von E. Doering, W. R. Roth,* and *G. Schröder,* J. Am. Chem. Soc. *95*, 8605 (1973).
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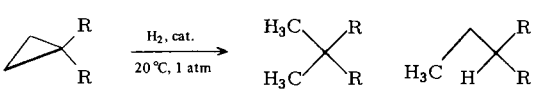
[7] The author is grateful to Ms. *U. Hackstein* for her assistance.

Selective Hydrogenations of 1,1-Disubstituted Cyclopropanes[**]

By *Claus Gröger* and *Hans Musso*[*]

The influence of substituents on cyclopropane bonds has been established experimentally and treated theoretically[2], particularly in the case of the norcaradiene-cycloheptatriene equilibrium. If there is p overlap between the substituent and the Walsh orbitals of the cyclopropane, electron-donating groups weaken the opposite C^2—C^3 bond, whereas electron-withdrawing groups strengthen it. The weakest bond in cyclopropane derivatives should be broken fastest on hydrogenolysis[1]. Neglecting steric effects of the substituents, these electronic factors should determine which bond this will be.



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

Table 1. Catalytic hydrogenation of cyclopropane derivatives *(1)* to give *(2)* or *(3)* over Pd/C (methanol) [3].

	R	Conditions	Product
(1a)	CH_3	incomplete	*(2a)*
(1a)	CH_3	72 h over PtO_2 (glacial acetic acid)	*(2a)*
(1b)	CH_2OH	185 atm, 24 h	*(2b)*
(1c)	CO_2CH_3	20 h	*(3c)*
(1d)	$CO_2C_2H_5$	20 h	*(3d)*
(1e)	CO_2H	20 h	*(3e)*
(1f)	$CONH_2$	20 h or 185 atm, 12 h	*(3f)*
(1g)	CN	6 h	*(3g)*, *(4)*

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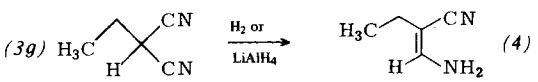
[**] Hydrogenolysis of Small Ring Compounds, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. All new compounds gave correct elemental analyses and spectra.—Part 3: ref. [1].

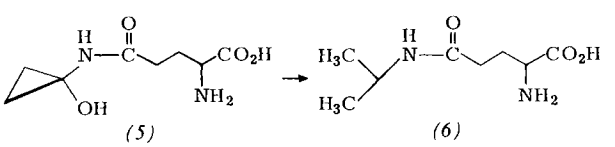
This control is clearly demonstrated by hydrogenation of several 1,1-disubstituted cyclopropane derivatives *(1)* with Pd/C (methanol) or PtO_2 (acetic acid)[3] catalyst to either 2,2-disubstituted *(2)* or 1,1-disubstituted propanes *(3)* respectively (Table 1).

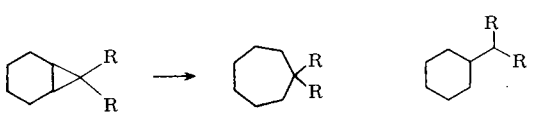
1,1-Dimethylcyclopropane *(1a)* and 1,1-cyclopropanedimethanol *(1b)* provide neopentane *(2a)* and 2,2-dimethyl-1,3-propanediol *(2b)*. The corresponding dimethyl and diethyl dicarboxylates *(1c)* and *(1d)*, the acid *(1e)*, and the amide *(1f)* are hydrogenated to the 2-ethylmalonates *(3c)*—*(3f)* exclusively. The absence of the isomeric compounds in the various products was proven by VPC and NMR with authentic samples of *(3a)* and *(3b)* as well as *(2c)*—*(2f)*[4]. The dinitrile *(1g)* takes up two moles of hydrogen, and forms 3-amino-2-ethylacrylonitrile *(4)*, identified by comparison with the known reduction product of *(3g)* with $LiAlH_4$[5]. Samples taken during hydrogenation of *(1g)* after consumption of one mole of hydrogen contained up to 30% of *(3g)* but no *(2g)*.



There are many examples[6] which can be interpreted in the same way, even though p overlap of alkyl groups is hard to understand. Other cases do not fit into this scheme. Thus, according to ref. [6], *(1a)* affords *(3a)* instead of *(2a)*. Since increasing temperature causes loss of selectivity[8], such hydrogenations should be carried out at room temperature or the lowest temperature possible, if necessary under pressure.

Some of these reactions are useful preparative methods, *e.g.* for the synthesis of geminal dimethylcycloalkanes[7, 8]. The specific ring opening in the hydrogenation of coprine *(5)*[9] to *(6)* also finds a lucid explanation.





(7a), R = CH_3 *(8a)* *(9b)*

(7b), R = CO_2R

Additionally, ring enlargement of a 7,7-dimethylbicyclo[4.1.0]heptane derivative *(7a)* to *(8a)* has been observed[10]. In contrast, the diester *(7b)* afforded cyclohexylmalonic ester *(9b)* exclusively[11]. In bicyclo[*n*.1.0]alkanes, however, the ratio of both alternatives, *viz.* *(8)* and *(9)*, crucially depends on the ring size *n*[12].

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(1a), 1630-94-0; *(1b)*, 39590-81-3; *(1c)*, 6914-71-2; *(1d)*, 1559-02-0; *(1e)*, 598-10-7; *(1f)*, 1559-03-1; *(1g)*, 5813-85-4; *(2a)*, 463-82-1; *(2b)*, 126-30-7; *(3c)*, 26717-61-9; *(3d)*, 133-13-1; *(3e)*, 601-75-2; *(3f)*, 6082-49-1; *(3g)*, 3696-37-5; *(4)*, 52698-15-4; *(5)*, 58919-61-2; *(6)*, 4311-12-0; *(7a)*, 1460-19-1; *(8a)*, 13151-49-0

[1] *B. Deppisch, H. Guth, H. Musso*, and *E. Ōsawa*, Chem. Ber. *109* (1976), in press.

[2] *R. Hoffmann*, Tetrahedron Lett. *1970*, 2907; *H. Günther*, Tetrahedron Lett. *1970*, 5173; *F. G. Klärner, ibid. 1974*, 19; *R. Hoffmann* and *W. D. Stohrer*, J. Am. Chem. Soc. *93*, 6941 (1971); *A. H. Andrist, ibid. 95*, 7531 (1973).

[3] 10% Palladium on charcoal: Merck Darmstadt. PtO_2: Degussa, Hanau.

[4] *(3a)*, *(3b)*, and *(2f)*: NMR <1%; *(2c)*, *(2d)*, *(2e)* not detectable in VPC <0.1%.

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[9] *P. Lindberg, R. Bergmann*, and *B. Wickberg*, J. Chem. Soc. Chem. Commun. *1975*, 946.

[10] *W. Cocker, P. V. R. Shannon*, and *P. A. Staniland*, Chem. Commun. *1965*, 254.

[11] *H. Musso*, Chem. Ber. *101*, 3710 (1968).

[12] *K.-J. Stahl* and *H. Musso*, to be published.

Structure of the "True" Metavanadate Ion

By *Joachim Fuchs, Soroush Mahjour*, and *Joachim Pickardt*[*]

Dedicated to Professor Georg Manecke on the occasion of his 60th birthday

Numerous studies[1a] on the size and structure of the isopolyvanadate ion occurring in aqueous vanadate(V) solutions at $Z \approx 1$[1b] (pH ≈ 7) have lead to contradictory conclusions. The various proposals include linear or cyclic trivanadate or tetravanadate ions having tetra- or penta-coordinate vanadium. Structural investigations on salts crystallizing from such solutions have so far failed to provide information relevant to the dissolved state because crystallization from aqueous solution is always accompanied by polymerization of the anion. Thus the anions of anhydrous alkali metal "metavanadates" are composed of VO_4 tetrahedra linked together as endless chains (diopside or spodumene type)[2]. $KVO_3 \cdot H_2O$, $Ca(VO_3)_2 \cdot 2H_2O$[2], and $Sr(VO_3)_2 \cdot 4H_2O$[3] contain chains of edge-linked VO_5 units.

Reaction of V_2O_5 with alcoholic tetrabutylammonium hydroxide solution[4] has now afforded the first isopolyvanadate of "metavanadate" type containing a discrete polyanion, *viz.* $[N(C_4H_9)_4]_3HV_4O_{12}$. This hydrogen tetravanadate is readily soluble in many organic solvents. Osmometric determinations in chloroform revealed a molecular mass of 1210 ($M_{calc.} = 1124$). Single crystals can be grown from solutions in acetone by addition of benzene; they can be stored for some time under the mother liquor or under anhydrous benzene. The intensities of 1630 nonequivalent reflections were measured on a single crystal in a sealed tube under benzene with a Syntex four-circle diffractometer. The compound crystallizes in the space group $P2_1/c$ with the lattice parameters $a = 12.347 \pm 0.005$, $b = 24.463 \pm 0.005$, $c = 23.236 \pm 0.005$ Å; $\beta = 92.476 \pm 0.05°$; $V = 7011.6$ Å^3; $Z = 4$. The vanadium positions were determined by direct methods, and those of the light atoms by successive difference Fourier syntheses. Owing to the unfavorable experimental conditions and a certain degree of disorder of the carbon atoms (terminal groups of the butyl chains) refinement was only possible up to $R = 12.8$%.

The anion proves to be a ring made up of four corner-linked VO_4 tetrahedra (Fig. 1) resembling the tetrametaphosphate[5] and the cyclotetrasilicate ion[6]. The four bridging O atoms form a square, the V atoms lying alternately above and below this plane (symmetry of ring nearly D_{2d}).

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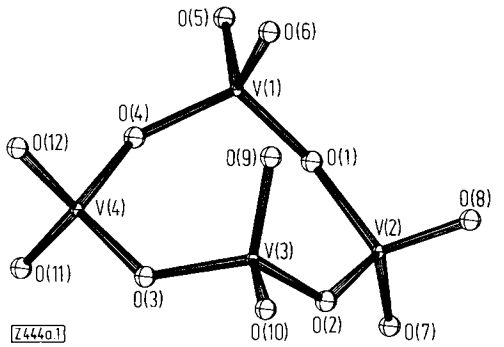

Fig. 1. Anion structure of tetrabutylammonium hydrogen tetravanadate $[N(C_4H_9)_4]_3HV_4O_{12}$.

The distances between the bridging O atoms and vanadium have an average value of 1.80 Å and those between vanadium and the terminal O atoms, except O(9), 1.62 Å. The oxygen atom O(9) is conspicuous for its high temperature factor and its significantly longer V—O distance (1.86 Å); it apparently exists (preferentially) in protonated form. The nitrogen atoms of the cations assume an approximately octahedral arrangement around the polyanion. ^{1}H-NMR measurements in deuteriochloroform show the OH proton to undergo extremely ready exchange (signal at -3.99 ppm).

The Raman spectrum of the tetrabutylammonium salt resembles the spectrum of an alkali metal vanadate solution that has acidified up to the "metavanadate" level ($Z=1$), thus indicating that such solutions also contain the cyclic tetravanadate ion. The polarized bands correspond to totally symmetric vibrations of terminal (947 cm^{-1}) and bridging (477 cm^{-1}) oxygen atoms and of the vanadium atoms (325 cm^{-1}). The bands at 920 and 628 cm^{-1} are assigned to asymmetric vibrations of terminal and bridging oxygen atoms. The symmetrical VOV stretching vibration is expectedly split in the solid state spectrum (512 and 471 cm^{-1}); the angles V(1)—O(1)—V(2) and V(1)—O(4)—V(4) are 132°, the angles V(2)—O(2)—V(3) and V(3)—O(3)—V(4) 146°. The Raman spectrum of a sodium "metavanadate" solution remains unchanged even at high dilutions (up to 4×10^{-3} M in V); there is no evidence for a concentration-dependent equilibrium between tetravanadate and trivanadate ions[7].

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CAS Registry number:
$[N(C_4H_9)_4]_3HV_4O_{12}$, 59005-33-3

[1] a) Gmelins Handbuch der Anorganischen Chemie, Syst.-No. 48, Vol. 1, pp. 149ff. (1967). b) Z is the ratio of reacted H^+ ions to the number of HVO_4^{2-} originally present. At $Z=1$, $H_2VO_4^-$ is formally present which is formally converted into VO_3^- by elimination of H_2O (formation of "meta-acid").
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Anion Structure of Tetrabutylammonium Octamolybdate $[N(C_4H_9)_4]_4Mo_8O_{26}$

By *Joachim Fuchs* and *Hans Hartl*[*]

Addition of an alcoholic solution of tetrabutylammonium hydroxide to a solution of tetrabutylammonium hexamolybdate $[N(C_4H_9)_4]_2Mo_6O_{19}$ in acetone leads to crystallization of the octamolybdate $[N(C_4H_9)_4]_4Mo_8C_{26}$. The same compound is obtainable in finely crystalline form on treatment of a slightly acidified aqueous solution of sodium molybdate with tetrabutylammonium bromide.

We have solved the structure by X-ray methods on the basis of 3295 nonequivalent reflections measured with a Syntex four-circle diffractometer and refined it to an R value of 5.5 %. In the monoclinic arrangement $P2_1/n$ the compound has the lattice parameters $a=15.086\pm0.003$, $b=15.997\pm0.003$, $c=18.528\pm0.003$ Å; $\beta=91.31\pm0.01°$; $Z=2$.

The centrosymmetric anion consists of a ring made up of six MoO_6 octahedra (as in $TeMo_6O_{24}^{6-}$[1]) linked to one MoO_4 tetrahedron above, and another below, its octahedral cavity (Fig. 1a). However, in view of the widely varying molybdenum-oxygen distances it can also be viewed as a loose addition compound between two MoO_4^{2-} units and a (neutral) Mo_6O_{18} ring made up of distorted MoO_4 tetrahedra. The distances between the Mo atoms and the terminal oxygen atoms O(7) to O(13) range from 1.667 to 1.692 Å, and the distances to the bridging atoms O(4) to O(6) from 1.881 to 1.917 Å. The distances of the tricoordinated atoms O(1) to O(3) (Fig. 2) of the MoO_4^{2-} units to the Mo atoms of the ring are unusual (2.35 to 2.53 Å) and correspond to bond orders of 0.35 to 0.2[2]. Mo(1) is in an almost ideal tetrahedral coordination with the O—Mo(1)—O angles between 108.1 and 110.6°. The distances between adjacent Mo atoms within the ring are 3.378 to 3.409 Å the distances between these atoms and Mo(1) 3.770 to 3.8 6 Å, and the distance Mo(1)—Mo(1′) 3.697 Å. The standard deviations are <0.001 Å for the Mo—Mo distances and <0.01 Å for the Mo—O distances.

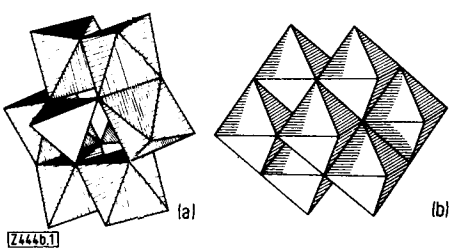

Fig. 1. Polyhedral structural model of $Mo_8O_{26}^{4-}$ in the tetrabutylammonium salt (a) and in the ammonium salt (b)

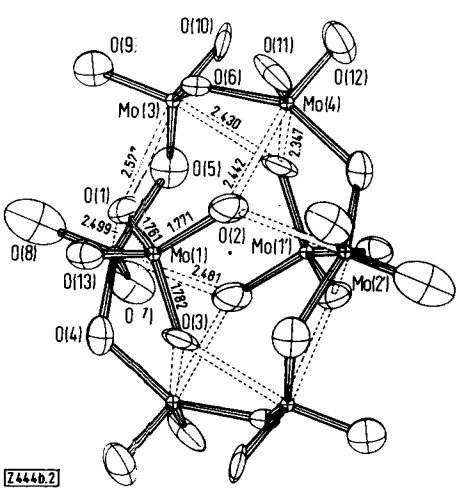

Fig. 2. Anion structure of tetrabuty ammonium octamolybdate; distances in Å.

This anion is an isomer of the anion occurring in ammonium octamolybdate $(NH_4)_4Mo_8O_{26}\cdot4H_2O$[3] which is made up solely of MoO_6 octahedra (cf. Fig. 1). Thus the present struc-

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tural elucidation provides the first proof of structural isomerism in discrete isopolyanions. In solution (*e.g.* in acetonitrile) tetrabutylammonium octamolybdate readily transforms into the hexamolybdate $[N(C_4H_9)_4]_2Mo_6O_{19}$. The bonding situation suggests that the mere approach of a negative charge to the oxygen atom O(13) can lead to the release of a MoO_4^{2-} unit. The structure provides an indication of the addition and elimination mechanisms involved in the formation and mutual interconversion of polyions.

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CAS Registry number:
$[N(C_4H_9)_4]_4Mo_8O_{26}$, 59054-50-1

[1] *H. T. Evans Jr.*, J. Am. Chem. Soc. *90*, 3275 (1968).
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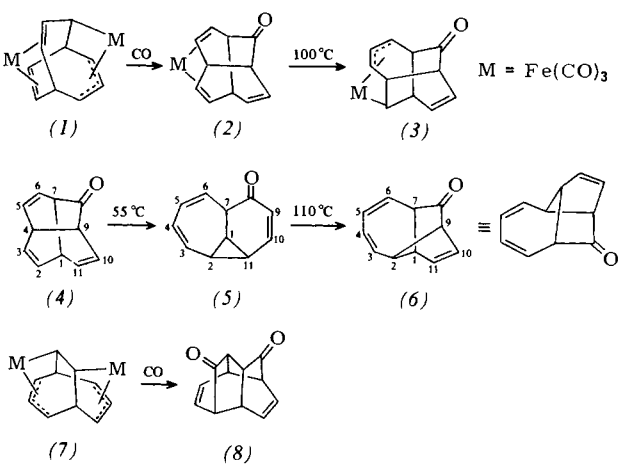
$C_{12}H_{10}O_2$ and Thermolabile $C_{11}H_{10}O$ Ketones from Bullvalene *via* Carbonyliron Complexes[1]

By *Rudolf Aumann*[*]

In the past few years synthetic methods have been reported in which highly reactive organic molecules (carbenes, cyclobutadiene, trimethylenemethane, norbornadienone[2]) have been initially stabilized by coordination to metal atom centers and subsequently liberated from the complex by a change in the oxidation state of the metal or displacement reactions and induced to undergo reaction.

Such a process permitted preparation of the tetracyclic diketone *(8)* and the thermolabile tricyclic monoketone *(4)* from bullvalene *via* the readily accessible carbonyliron complexes *(1)* and *(7)*[3]. Compound *(4)* and the products of its thermal isomerization *(5)* and *(6)* are new representatives of the $C_{11}H_{10}O$ ketones[4], which possess theoretical interest.



(1) *(2)* *(3)* *(4)* *(5)* *(6)* *(7)* *(8)*

Carbonylation of *(1)* (100 atm of CO, 75°C, 24 h) leads to displacement[5] of the π-allyl/σ-bonded $Fe(CO)_3$ group affording the mononuclear carbonyliron complex *(2)* [80%; yellow crystals, m.p. 100—102°C; $m/e = 298$; IR (hexane): ν(C≡O) 2039, 1977, 1966 cm^{-1}; IR (KBr): ν(>C=O) 1710 cm^{-1}]. Oxidative decomposition of *(2)* with $FeCl_3$ in ether (0°C, 10 min) gives tricyclo[5.4.0.0^{4,9}]undeca-2,5,10-trien-8-one *(4)* [80%; colorless crystals from benzene/hexane, m.p. 80°C; $m/e = 158$; ^{1}H-NMR ($CDCl_3$): $\tau = 3.39$ (dd, H-5, H-11; $J = 6$, 8.5 Hz), 4.06 (AA'XX' system, H-2, H-3), 4.39 (dd, H-6, H-10; $J = 8$, 8.5 Hz), 7.0 ("t", H-7, H-9; $J = 8$, 8 Hz), 7.3 (m, X part of an AA'XX' system, H-1, H-4); ^{13}C-NMR ($CDCl_3$): δ_{TMS}(>C=O) = 206.3 ppm; IR (KBr): ν(>C=O) 1700 cm^{-1}].

In contrast to the carbonyliron complex *(2)* of the ketone *(4)*, which slowly rearranges at 100°C to *(3)* [95% in 3 d; colorless crystals, m.p. 115—117°C; $m/e = 298$; IR (hexane): ν(C≡O) 2054, 1986 cm^{-1}; IR (KBr) ν(>C=O) 1720 cm^{-1}], free *(4)* already isomerizes slowly in solution at 25°C, and quantitatively within 1 h at 55°C by Cope rearrangement to give tricyclo[5.4.0.0^{2,11}]undeca-3,5,9-trien-8-one *(5)* [colorless crystals from hexane, m.p. 47°C; $m/e = 158$; ^{1}H-NMR ($CDCl_3$): $\tau = 3.02$ (dd, H-10; $J = 6$, 10 Hz), 3.56 (dd, H-6, $J = 8$, 11 Hz), 3.9—4.1 (m, H-4, H-5), 4.02 (d, H-9; $J = 10$ Hz), 4.35 (dd, H-3; $J = 11$, *ca.* 3 Hz), 6.80 (dd, H-7; $J = 7.5$, 8 Hz), 7.66 ("q", H-1; $J = 7.5$, 7.5, 7.5 Hz), 7.93 (ddd, H-2; $J = 7.5$, 8, *ca.* 3 Hz), 8.46 (ddd, H-11; $J = 6$, 7.5, 8 Hz); ^{13}C-NMR ($CDCl_3$): δ_{TMS}(>C=O) = 196.5 ppm; IR (KBr): ν(>C=O) 1660 cm^{-1}].

At 110°C compound *(5)* isomerizes cleanly *via* a vinylcyclopropane/cyclopentene rearrangement (*ca.* 95% in 1 h) to tricyclo[5.4.0.0^{2,9}]undeca-3,5,10-trien-8-one *(6)* [colorless crystals from pentane, m.p. 40°C; $m/e = 158$; ^{1}H-NMR ($CDCl_3$): $\tau = 3.12$ (dd, H-11; $J = 5.5$, 3.0 Hz), 3.72 (dd, H-10) $J = 5.5$, 3.5 Hz), 3.7 to 4.3 (m, H-3, H-4, H-5, H-6), 6.55 ("s", H-7), 6.9—7.2 (m, H-2, H-9), 7.43 ("s", H-1); ^{13}C-NMR ($CDCl_3$): δ_{TMS}(>C=O) = 210.0 ppm; IR (KBr): ν(>C=O) 1735 cm^{-1}].

The tetracyclic diketone *(8)* [colorless crystalline needles, m.p. 208°C; $m/e = 186$; ^{1}H-NMR ($CDCl_3$): $\tau = 3.84$ (dd, 2H; $J = 8.0$, 8.0 Hz), 4.15 (dd, 2H; $J = 6.0$, 8.0 Hz), 6.55 (m, M part of an AA'MM' system, 2H), 7.36 ("dd", 2H; $J = 7.5$, 8.0 Hz), 7.52 (A part of an AA'MM' system, 2H); ^{13}C-NMR ($CDCl_3$): δ_{TMS}(>C=O) = 208.7 ppm; IR (KBr): ν(>C=O) 1735 cm^{-1}] is obtainable in quantitative yield by carbonylation of *(7)*[3] (100 atm of CO, 80°C, 2 d).

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CAS Registry numbers:
(1), 35443-07-3; *(2)*, 58312-76-8; *(3)*, 58312-77-9; *(4)*, 58298-58-1; *(5)*, 58298-59-2; *(6)*, 58298-60-5; *(7)*, 35443-09-5; *(8)*, 58298-61-6; bullvalene, 1005-51-2

[1] Part 3 of the series: Organic Syntheses with Transition Metal Complexes. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 2: ref. [5b].
[2] Cf., *e.g.*, *E. O. Fischer*, Angew. Chem. *86*, 651 (1974); *G. F. Emerson, L. Watts*, and *R. Pettit*, J. Am. Chem. Soc. *87*, 131 (1965); *J. M. Landesberg* and *J. Sieczkowski*, *ibid. 91*, 2120 (1969); *G. F. Emerson, K. Ehrlich, W. P. Giering*, and *P. C. Lauterbur*, *ibid. 88*, 3172 (1966).
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Na_3NO_3—Not an Orthonitrite

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So far it has remained unclear whether Na_3NO_3[1,2] exists as a salt of "orthonitrous acid" or as an adduct $Na_2O \cdot NaNO_2$; cryoscopic investigations in molten $LiNO_3$ and in an $LiNO_3/KNO_3$ eutectic indicate existence of the anion NO_3^{3-}[2].

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We obtained Na_3NO_3 in the form of a golden-yellow, microcrystalline, moisture-sensitive powder by heating equimolar quantities of Na_2O[3] and $NaNO_2$ (Merck, dried by melting *in vacuo*) in a sealed silver crucible (310°C, 3d).

The X-ray power diagrams contain few lines and can be completely indexed for a primitive cubic structure, $a=4.605(3)$ Å (Guinier data). A structural model was found by "trial and error" which led to very good agreement between calculated and observed line intensities (21 Debye-Scherrer lines): space group $Pm3m\text{-}O_h^1$; $Z=1$; O_I at 1 (a), Na at 3 (d), the NO_2^- group centered about 1 (b). If the known geometry of the nitrite ion[4] is retained, examination of the bond distances shows that the most favorable orientation for the NO_2^- fragment arises when the interatomic contacts O...O coincide with one of the [100]~ directions (cf. Fig. 1). Accordingly N and O_{II} occupy the equivalent position 6(f) with $x=0.37$, occupation factor = 1/6 for N and $x=0.27$, occupation factor = 1/3 for O_{II}.

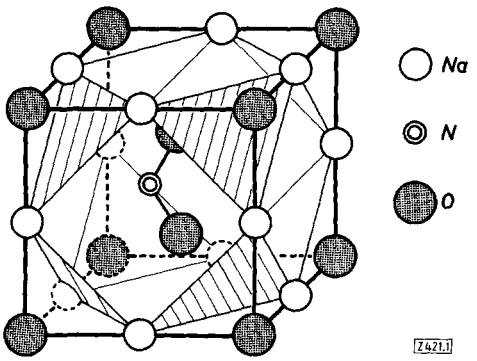

Fig. 1. Crystal structure of Na_3NO_3 (the NO_2^- group is shown in one of the possible orientations).

On the strength of this postulated structure the crystal structure of Na_3NO_3 is derived of the anti-perowskite type corresponding to the formulation $[NO_2^-]ONa_3$ and contains *no* NO_3^{3-} groups. In the meantime a single crystal of Na_3NO_3 has also been obtained; data collection for [100], [110], and [111] confirm the dimensions and symmetry (Laue group m3m).

Single crystal data ought to provide more detailed information about the structure (*e.g.* whether orientation disorder or hindered rotation of the NO_2^- anion occur).

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CAS Registry number:
Na_3NO_3, 58904-50-0

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Arsenic Pentachloride, $AsCl_5$[**]

By *Konrad Seppelt*[*]

Fourth-row nonmetals exhibit striking anomalies (instability) in their highest valency states. The best known example is provided by the late discovery of the perbromates[1]; and another may be seen in the phenomenon that both phosphorus pentachloride and antimony pentachloride have long been known but not arsenic pentachloride, although the first attempted preparation was described as early as 1834[2]. Meanwhile there has been no lack of attempts to close that gap[3]. It has now proved possible to detect $AsCl_5$.

Irradiation of a solution of $AsCl_3$ in chlorine with UV light at −105°C affords arsenic pentachloride.

$$AsCl_3 + Cl_2 \underset{-50\,^\circ C}{\overset{-105\,^\circ C,\ h\nu}{\rightleftharpoons}} AsCl_5$$

Gravimetric analysis of the reaction product indicated the composition $AsCl_{4.9}$. Unequivocal identification was accomplished by Raman spectroscopy: the bands of $AsCl_3$ [405, 370, 194, 158 cm^{-1}] disappear and new absorptions [437, 369 (p), 295 (p), 220, 213, 83 cm^{-1}] appear, which on account of their position, intensity, and polarization can only be assigned to $AsCl_5$. This is particulary clear on comparison with the spectra of PCl_5 and $SbCl_5$[4] (see Fig. 1).

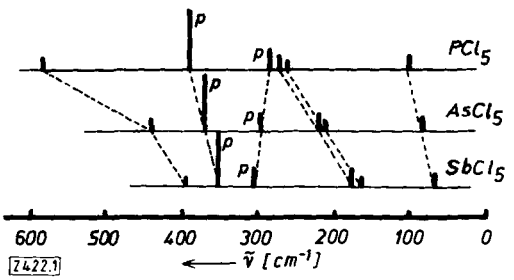

Fig. 1. Raman spectra of the pentahalides ECl_5.

Presumably due to entrained chlorine $AsCl_5$ is a pale yellow solid; it melts with partial decomposition at about −50°C.

The Raman spectrum not only confirms the existence of $AsCl_5$ but also provides structural information. In solution the molecule has a trigonal-bipyramidal structure, as do PCl_5 and $SbCl_5$ in the liquid or dissolved state. However, the same structure is retained in the solid state, *i.e.* the compound does not adopt an ionic structure like that of solid PCl_5 ($=PCl_4^+PCl_6^-$)[5] or dimerize like solid $SbCl_5$ ($=Cl_4SbCl_2SbCl_4$)[6]. It cannot be ruled out though that such transformations may occur very slowly owing to the low temperature.

A cursory consideration of the Raman spectrum also reveals that the As—Cl bonds are no weaker than the P—Cl and Sb—Cl bonds. The instability of $AsCl_5$ must therefore have other reasons. Although the formation reaction is clearly a radical chlorination it can be formally resolved into the following steps:

$$AsCl_3 \xrightarrow{-e} AsCl_3^+ \xrightarrow{+Cl^-} AsCl_4^+ \xrightarrow{+Cl^-} AsCl_5$$

The overall enthalpy of reaction amounts to −22.1 kcal/mol for PCl_5(g) and −17.0 kcal/mol for $SbCl_5$(g). Since formation of the two new arsenic-chlorine bonds should involve approximately the same amount of energy as in the case of phosphorus and antimony the difference must be attributed to the differing ionization energies in the first step of the reaction. Indeed, the ionization of $AsCl_3$ (11.7 eV) is 27.5 kcal/mol higher than that of PCl_3 (10.5 eV)[7]; this energy difference suffices to make the reaction endothermic.

From the vantage point of bond theory the higher ionization energy of $AsCl_3$ will of course mean that the promotion energy into an excited state will also be raised accordingly, *i.e.* $E_{4s\rightarrow 4p,d} > E_{3s\rightarrow 3p,d}$. This unexpected sequence is a consequence of

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the *transition metal contraction*: the slight screening of the relatively large nuclear charge of As(Se,Br) by the 3d electrons lowers the 4s orbital, the nonbonding electron pair in $AsCl_3$ having pronounced s character (bond angle 98°). While the situation has become normal again for Sb (Te, I, Xe), the same phenomenon occurs once more in the case of Bi *(lanthanoid contraction)*. This explains why $BiCl_5$ is also still unknown and probably even less stable than $SbCl_5$.

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German version: Angew. Chem. *88*, 410 (1976)

CAS Registry numbers:
$AsCl_5$, 22441-45-8; $AsCl_3$, 7784-34-1

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[2] *J. Liebig* and *F. Wöhler*, Justus Liebigs Ann. Chem. *11*, 150 (1834).
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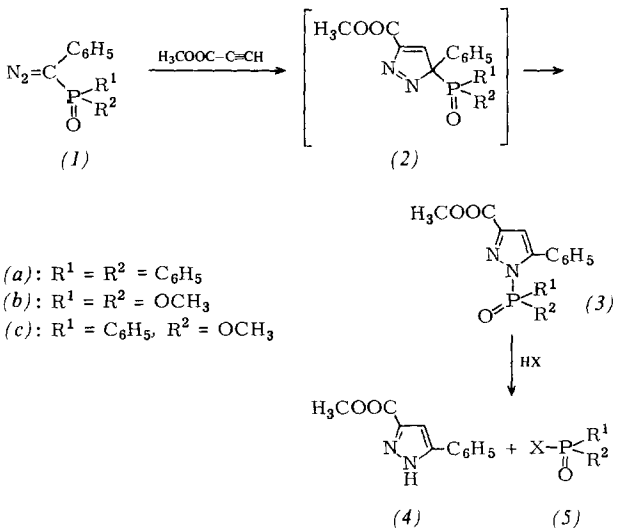
Phosphorylation with 1-Phosphorylpyrazoles[**]

By *Utz Felcht* and *Manfred Regitz*[*]

The phosphoryldiazoalkanes *(1a)*—*(1c)*[1] add regiospecifically to methyl propiolate to give the 3*H*-pyrazoles *(2a)*—*(2c)*, in which the phosphoryl group undergoes a spontaneous [1,5] shift to give the 1-phosphorylpyrazoles *(3a)*—*(3c)* (77—100 %)[2]. These compounds, which can be stored almost indefinitely at 0 °C in the absence of moisture, are suitable reagents for the phosphorylation of, *inter alia*, alcohols, enols, phenols, oximes, amines, α-amino acid esters, hydrazines and azides (see Table 1). This reaction, which can be formulated as *(3)* + HX → *(4)* + *(5)*, is reminiscent of acylation reactions with azolides[3].



(a): $R^1 = R^2 = C_6H_5$
(b): $R^1 = R^2 = OCH_3$
(c): $R^1 = C_6H_5$, $R^2 = OCH_3$

Characteristic of this method are the mild reaction conditions, satisfactory yields of products (see Table 1), and the potential variability of phosphoryl substituents and reaction partners. The problems met with in phosphorylation with difficultly handleable phosphoryl chlorides, which at least in the case of alcohols necessitates employment of auxiliary bases, are not encountered. In particular, the reaction with *(3c)* has proven to be far superior to that with the methyl ester of

Table 1. Phosphorylation of alcohols, enols, phenols, oximes, amines, α-aminocarboxylates, hydrazines and azides with 1-phosphorylpyrazoles *(3)* (typical examples).

Educt (HX)	Solvent	Reaction conditions T [°C]	t [h]	Product *(5)*	Yield [%]	B.p. [°C/torr] [a] M.p. [°C]
$(H_3C)_2CH-OH$	—	25	12	$(H_3C)_2CH-O-P(OCH_3)_2$ (O)	77	90/0.06
$HO-CH_2-CH_2-OH$	—	50	12	$HO-CH_2-CH_2-O-P(OCH_3)(C_6H_5)$ (O)	76	not distillable
$H_3C-C(=O)-CH=C(OH)-CH_3$	acetonitrile [b]	25	10	$H_3C-C(=O)-CH=C(O-P(O)(C_6H_5)_2)-CH_3$	47	74—77 (ether/*n*-hexane, 1:3)
C_6H_5OH	acetonitrile	78	30	$C_6H_5-O-P(OCH_3)(C_6H_5)$ (O)	73	124/0.1
$(H_3C)_2C=N-OH$	acetonitrile	78	5	$(H_3C)_2C=N-O-P(OCH_3)(C_6H_5)$ (O)	53	140/0.06
$(H_3C)_2NH$	benzene	25	1	$(H_3C)_2N-P(OCH_3)(C_6H_5)$ (O)	72	130/0.01
	benzene	25	6d		38	83 (ether)
$H_5C_2OOC-CH_2-NH_2$	benzene	25	12	$H_5C_2OOC-CH_2-NH-P(OCH_3)(C_6H_5)$ (O)	45	190/0.03
H_2N-NH_2	tetrahydrofuran	25	0.5	$H_2N-NH-P(OCH_3)_2$ (O)	89	73—74 (benzene)
NaN_3	tetrahydrofuran/water	0	2	$N_3-P(OCH_3)(C_6H_5)$ (O)	36	95/0.01

[a] Oven temperature during bulb-tube distillation; [b] $N(C_2H_5)_3$-addition. All compounds gave correct analyses.

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phenylphosphonic chloride[4]. Amines can be phosphorylated even in an aqueous medium without *(3)* being hydrolyzed. The usual workup under anhydrous conditions precludes reaction products sensitive to hydrolysis.

Typical procedure

A solution of *(3c)* (7.1 g, 20 mmol) in methylallyl alcohol/anhydrous acetonitrile (5 ml/50 ml) is heated for 12 h under reflux in the absence of moisture. On cooling to 0 °C, *(4)* crystallizes out (m. p. 138 °C; Ref. [5]: 181—182 °C). The filtrate is concentrated by evaporation at 30 °C/12 torr, the residue taken up in ether (20 ml), and the resulting solution chromatographed on activated charcoal (Merck, 0.5—0.75 mm; column length 50 cm, diameter 3 cm) with 3000 ml ether. The phosphonic ester obtained after removal of solvent by evaporation at 25 °C/12 torr is already thin-layer chromatographically homogeneous; it is finally isolated by bulb-tube distillation at 120 °C (oven temperature)/0.03 torr; yield 3.4 g (75 %). IR (film): 1600 (C=C), 1450 (P-phenyl), 1625 (PO), 1020 cm^{-1} (P—O—C). ^{1}H-NMR ($CDCl_3$): τ = 4.85—5.17 (m, olefinic CH_2), 5.53 (d, $^3J_{P,H}$ = 8.0 Hz, OCH_2), 6.25 (d, $^3J_{PH}$ = 11.0 Hz, OCH_3), 8.25 ppm (m, CH_3-allyl). The elemental analysis is correct.

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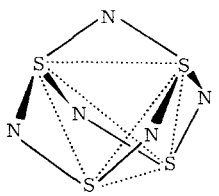
CAS Registry numbers:
(3a), 56426-26-7; *(3b)*, 56426-22-3; *(3c)*, 58816-54-9; *(4)*, 56426-35-8; methyl methylallyl phenylphosphonate, 58816-55-0; Table 1: Educts (from top to bottom), 67-63-0; 107-21-1; 1522-20-9; 108-95-2; 127-06-0; 124-40-3; 110-91-8; 459-73-4; 302-01-2; 26628-22-8; Table 1: Products *(5)* (from top to bottom), 58816-56-1; 58816-57-2; 58816-58-3; 55638-42-1; 58816-59-4; 55215-28-6; 55025-89-3; 58816-60-7; 58816-61-8; 58816-62-9; methylallyl alcohol, 513-42-8

[1] *(1a)*: *M. Regitz* and *W. Anschütz*, Chem. Ber. *102*, 2216 (1969); *(1b)*: *H. Scherer, A. Hartmann, M. Regitz, B. D. Tunggal*, and *H. Günther*, *ibid. 105*, 3357 (1972); *(1c)*: *U. Felcht* and *M. Regitz*, *ibid. 108*, 2040 (1975).
[2] *A. Hartmann* and *M. Regitz*, Phosphorus *5*, 21 (1974).
[3] *H. A. Staab*, Angew. Chem. *74*, 407 (1962); Angew. Chem. Int. Ed. Engl. *1*, 351 (1962).
[4] *K. Sasse* in Houben-Weyl-Müller: Methoden der organischen Chemie, Vol. XII/1. Thieme, Stuttgart 1963, p. 418, 612.
[5] *K. v. Auwers* and *C. Mansolf*, Ber. Deut. Chem. Ges. *60*, 1730 (1927).

Crystal and Molecular Structure of the Tetrasulfur Pentanitride Anion

By *Wolfgang Flues, Otto J. Scherer, Johannes Weiss*, and *Gotthelf Wolmershäuser*[*]

The structure of a S_4N_4 molecule with an additional N bridge was proposed for the recently discovered species $[S_4N_5]^-$[1]:



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The correctness of this assumption has now been confirmed by an X-ray structure analysis of $[R_4N]^+[S_4N_5]^-$ *(2)*, R = *n*-C_4H_9.

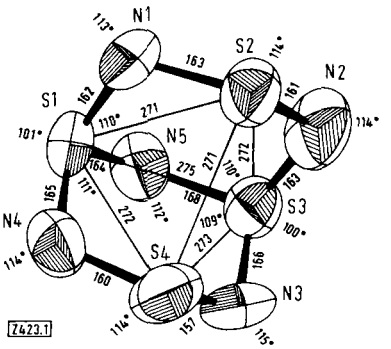

Fig. 1. Structure of $[S_4N_5]^-$ (distances in pm; the thermal ellipsoids correspond to a probability of 50 %).

Compound *(2)* forms monoclinic crystals having a = 1112.5(5), b = 1558.8(6), c = 1348.5(5) pm; β = 90.26(6)°; space group $P2_1/n$; Z = 4. Using Mo-K_α radiation with 2θ = 44° a total of 1307 independent reflections of intensity $I > 2.58\delta(I)$ were recorded on a diffractometer; since the crystal decomposes during the measurement the reflections had to be adjusted to the same level with the aid of a reference reflection. The data were corrected by standard methods. The structure was solved by direct methods and refined with anisotropic temperature factors to an R value of 11.1 %. The positions of the protons were not determined.

Figure 1 shows the S_4N_5 anion with bond lengths, bond angles, and also the S···S distances (standard deviations: S—N 2 pm, S···S 1 pm, angles 1°). Its structure closely resembles that of $[S_4N_5O]^-$[2]. The average value of the S—N bond lengths (163 pm) corresponds to that in S_4N_4 (162 pm)[3] and $[S_4N_5O]^-$ (162 pm)[2]. However, a significant deviation is seen in the maximum difference between the S···S distances: bridging of the fifth tetrahedral edge by a negatively charged N atom in the anion of *(2)* largely equalizes the S···S distances (almost undistorted S tetrahedron) so that approximately equal interactions are to be postulated between all the S atoms.

$[S_4N_5]^-$—the first binary sulfur-nitrogen anion whose structure has been elucidated—may possibly occupy a key position among the SN anions like $[S_4N_3]^+$ among the SN cations or S_4N_4 among the neutral species. In the same way as S_4N_4 corresponds formally to an inverted As_4S_4 structure, this also applies to $[S_4N_5]^-$ and As_4S_5[4] or β-P_4S_5[5].

In analogy with $[(CH_3)_3CNH_3]^+[S_4N_5]^-$[1], methanolysis[6] of *N,N'*-bis(trimethylsilyl)sulfur diimide leads to $[NH_4]^+[S_4N_5]^-$ *(1)*, which can be converted into $[R_4N]^+[S_4N_5]^-$ *(2)* with R_4NOH:

$$Me_3Si{-}N{=}S{=}N{-}SiMe_3 \xrightarrow{CH_3OH} \underset{(1)}{[NH_4]^+[S_4N_5]^-} \xrightarrow[-\,NH_4OH]{+\,R_4NOH}$$

R = n-C_4H_9 $\qquad$ $[R_4N]^+[S_4N_5]^-$ *(2)*

Compound *(2)*, which like *(1)* has been characterized by complete elemental analysis, and IR and mass spectrometry, can easily be examined by UV spectroscopy owing to its greater stability in methanol as compared with $[(CH_3)_3CNH_3]^+[S_4N_5]^-$: λ_{max} = 480 ($\log\varepsilon$ = 1.25), 343 (sh, 3.37), 285 nm (3.75).

Procedure:

(1): $[(CH_3)_3SiN]_2S$[7] (5.16 g, 0.025 mol) and methanol (12 ml, 0.3 mol) are stirred together at room temperature for *ca.* 0.5 h (evolution of gas!). The reaction product precipitated with benzene is filtered off (G3 frit), washed with benzene, and dried under oil-pump vacuum. A further crop of *(1)* precipitates from the filtrate within a few days. Yield 1.1 g (80 %, based on the stoichiometry given in ref. [6]).

(2): Compound *(2)* is formed as a yellow precipitate from an aqueous solution of *(1)* (0.8 g, 3.7 mmol) and $(n\text{-}C_4H_9)_4NOH$ (2.0 g, 7.7 mmol). Yield 1.3 g (80 %). Recrystallization from acetone/ethyl acetate (1 : 1) yields yellow needles.

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CAS Registry numbers:
(1), 58904-51-1; *(2)*, 58894-68-1; $[(CH_3)_3SiN]_2S$, 18156-25-7

[1] *O. J. Scherer* and *G. Wolmershäuser*, Angew. Chem. *87*, 485 (1975); Angew. Chem. Int. Ed. Engl. *14*, 485 (1975).
[2] *R. Steudel, P. Luger*, and *H. Bradaczek*, Angew. Chem. *85*, 307 (1973); Angew. Chem. Int. Ed. Engl. *12*, 316 (1973).
[3] *B. D. Sharma* and *J. Donohue*, Acta Crystallogr. *16*, 891 (1963).
[4] *H. J. Whitfield*, J. Chem. Soc. Dalton Trans. *1973*, 1740.
[5] *A. M. Griffin* and *G. M. Sheldrick*, Acta Crystallogr. *B31*, 2738 (1975).
[6] Mass balancing indicates the following overall equation:

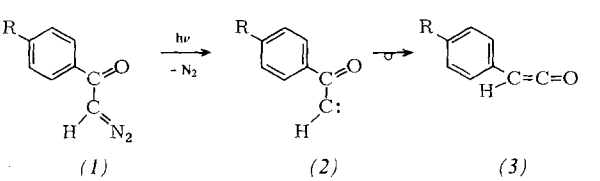
$$12[(CH_3)_3SiN]_2S + 24CH_3OH \rightarrow 3[NH_4]^+[S_4N_5]^- + 4NH_3 + N_2 + 24(CH_3)_3SiOCH_3$$

[7] *O. J. Scherer* and *R. Wies*, Z. Naturforsch. *25b*, 1486 (1970).

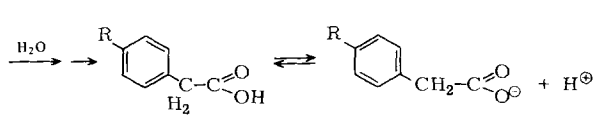
Rate of Acid Formation from Phenylketenes in Aqueous Solution

By *Eberhard Bothe, Herbert Meier, Dietrich Schulte-Frohlinde*, and *Clemens von Sonntag*[*]

We report here on the first measurement of the rate of acid formation from ketenes in aqueous solution. The difficulty met with in this measurement lies in the high rate of reaction of the ketene with water, thus necessitating both rapid preparation of the ketenes *in situ* as well as rapid measurement of acid formation.



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



(4) *(5)*

R = H, F, Cl, CH_3, OCH_3, CN, NO_2

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We prepared the ketenes *(3)* from *p*-substituted diazoacetophenones *(1)* *via* carbenes *(2)* by flash-photolytic Wolff rearrangement[1, 2]. On addition of water the ketenes *(3)* are converted into acids *(4)*, whose dissociation gives rise to conductive species *(5)*. The rate of increase of conductivity in solution was measured. The rise time of the electronic setup was 80 ns (the halfwidth of the photoflash being 5 µs). The increase of conductivity was found to be of first order over a duration of more than three halflives. The halflive was independent of the light intensity (factor of 50), of the initial concentration of diazoacetophenone, and of the pH in the range 4—10.8. The concentration of protons formed was between 8×10^{-8} and 4×10^{-6} mol/l. For R = H it was shown that the acid formed had the same pK as phenylacetic acid.

Table 1. Rate constants k of the formation of acids from 4-substituted phenylketenes *(3)* generated *in situ* from diazoacetophenones *(1)* at 26 °C in aqueous solution. $t_{1/2}$ = halflife, σ_p^n = Hammett substituent constant.

R in *(3)*	$t_{1/2}$ [µs]	k [10^3 s^{-1}]	σ_p^n [3]
NO_2	14	49.5	0.778
CN	27	25.6	0.674
Cl	72	9.6	0.238
F	117	5.9	0.056
H	141	4.9	0.000
OCH_3	152	4.5	−0.111
CH_3	184	3.8	−0.129

The rate-determining step for formation of the ions cannot be the dissociation of the acids *(4)*, because this would give a halflife of ≈1 µs. The elimination of nitrogen from *(1)* is limited by the lifetime of the electronically excited singlet state of the diazoketone and is therefore also too rapid. Nor can the rate of rearrangement of the carbenes be rate determining: the order of the relative rates of migration of the fragments is in the reverse order[2, 4] to that for the rates of acid formation (Table 1).

It was concluded previously that the photolytic Wolff rearrangement proceeded predominantly *via* an excited singlet carbene and must therefore take place within the lifetime of excited singlet states[2, 4]. This conclusion is supported by the fact that the presence of atmospheric oxygen does not influence the acid formation. Hence the increase in conductivity must be attributed to the formation of acids *(4)* from the ketenes *(3)*. Whether the ketene hydrate is involved in the formation of the acid is still unknown. It thus remains an open question whether addition of water to the ketene on rearrangement of the ketene hydrate into the acid is the rate determining step.

The formation of acid is surprisingly rapid. In the pH range investigated *viz.* 4—10.8, it is not catalyzed by $H^{\oplus}$ or $OH^{\ominus}$. The activation energy for *(1)*, R = Cl, is 9.3 kcal/mol (frequency factor $10^{10.72}$ s^{-1}). Acid formation from *(1)*. R = H or Cl, proceeds slower in D_2O than in H_2O by a factor of 2 or 1.8, respectively. The dependence on substituents conforms to a linear free energy relationship. Use of the Hammett equation with the constants σ_p^n[3] yields a value $\rho = 1.19$ (correlation coefficient 0.97). Thus, electron withdrawing substituents accelerate acid formation, electron repelling substituents retard it.

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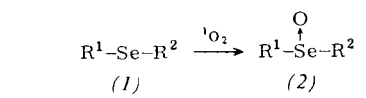
CAS Registry numbers:
(1) (R = NO_2), 4203-31-0; *(1)* (R = CN), 3490-50-4; *(1)* (R = Cl), 3282-33-5; *(1)* (R = F), 3488-44-6; *(1)* (R = H), 3282-32-4; *(1)* (R = OCH_3), 6832-17-3; *(1)* (R = CH_3), 17263-64-8; *(3)* (R = NO_2), 58784-38-6; *(3)* (R = CN), 58784-39-7; *(3)* (R = Cl), 58784-40-0; *(3)* (R = F), 58784-41-1; *(3)* (R = H), 3496-32-0; *(3)* (R = OCH_3), 58784-42-2; *(3)* (R = CH_3), 58784-43-3

[1] *W. Kirmse:* Carbene, Carbenoide und Carbenanaloge. Verlag Chemie, Weinheim 1969.
[2] *H. Meier* and *K.-P. Zeller*, Angew. Chem. *87*, 52 (1975); Angew. Chem. Int. Ed. Engl. *14*, 32 (1975).
[3] *H. van Bekkum, P. E. Verkade*, and *B. M. Wepster*, Rec. Trav. Chim. Pays-Bas *78*, 815 (1959); *A. J. Gordon* and *R. A. Ford:* The Chemist's Companion. Wiley, New York 1972.
[4] *K.-P. Zeller, H. Meier*, and *E. Müller*, Tetrahedron *28*, 5831 (1972).

Photo-Oxygenation of Selenides—A New Pathway to Selenoxides

By *L. Hevesi* and *Alain Krief*[*]

We have found that dialkyl and aryl alkyl selenides *(1)* are transformed by photochemically generated singlet oxygen[1] into selenoxides *(2)*[2] (see Table 1), which possess interesting synthetic applications[3].



(1) *(2)*

Table 1. Reactions of selenides with singlet oxygen to form selenoxides. See procedure for reaction conditions.

	R^1	R^2	Reaction time [h]	Yield [%]
a	C_6H_5	CH_3	7	95
b	C_6H_5	$CH_2C_6H_5$	2.5	70 (10) [a]
c	C_6H_5	C_3H_7—CHOH—CH(C_3H_7)	3.5	28 (45) [a, b]
d	CH_3	C_9H_{19}—CH(CH_3)	5	85 (10) [a]
e	CH_3	C_3H_7—CHOH—CH(C_3H_7)	4.5	70 (15) [a, c]

[a] Figures in parentheses refer to the amount of starting material recovered at the conclusion of the reaction.
[b] 27% of 5-octen-4-ol also formed.
[c] 15% of 5-octen-4-ol also formed.

The yields of selenoxides are very high; no selenone formation was observed in any of the reactions. In some cases the known thermal elimination of selenenic acids RSeOH occurred, leading to formation of olefins[3]. This was especially pronounced with β-hydroxy selenides which underwent partial conversion into allyl alcohols (Table 1). The yields of allyl alcohols increase with rising temperature and duration of irradiation. Thus the yield of 5-octen-4-ol from *(1e)* increases from 15% (20°C, 4.5 h) to 42% (50°C, 4.5 h), and that from *(1c)* increases from 27% (20°C, 3.5 h) to 46% (20°C, 17.5 h)[4]. This allyl alcohol is not oxidized on irradiation.

Procedure:

In a typical experiment, compound *(1)* (1 mmol) and Bengal rose (10 mg) are dissolved in anhydrous methanol (120 ml). Oxygen is passed through the stirred solution which is irradiated with a Sylvania iodine lamp (220 V, 650 W) operated at 135 V (≙325 W). The course of the reaction is monitored by thin-layer chromatography. After distillation of solvent the crude mixture is worked up by chromatography.—The products were identified by comparison (IR, ^{1}H-NMR) with authentic material.

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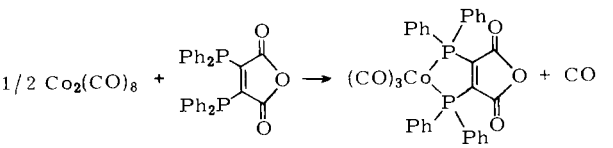
CAS Registry numbers:
(1a), 4346-64-9; *(1b)*, 18255-05-5; *(1c)*, 56414-33-6; *(1d)*, 58856-08-9; *(1e)*, 58873-23-7; *(2a)*, 25862-09-3; *(2b)*, 13154-11-5; *(2c)*, 58856-09-0; *(2d)*, 58856-10-3; *(2e)*, 58873-24-8; 5-octan-4-ol, 58856-11-4

[1] a) *G. O. Schenck*, Angew. Chem. *64*, 12 (1952); b) *R. W. Denny* and *A. Nickon*, Org. React. *20*, 133 (1973).
[2] For analogous reactions of sulfides see a) *G. O. Schenck* and *C. H. Krauch*, Chem. Ber. *96*, 517 (1963); b) *K. Gollnick*, EUCHEM Research Conference No. 69, Sept. 1975 at Ghent (Belgium).
[3] See, *e.g., H. J. Reich, J. M. Ranga*, and *I. L. Reich*, J. Am. Chem. Soc. *97*, 5434 (1975); references cited therein.
[4] On prolonged irradiation the selenide *(1)* decomposes with deposition of red selenium.

A Mononuclear Paramagnetic Biphosphinotricarbonylcobalt(0) Complex

By *Dieter Fenske*[*]

With few exceptions, such as $V(CO)_6$, carbonylmetal(0) complexes are diamagnetic. The same applies to their phosphane-substituted derivatives. We have now obtained a paramagnetic cobalt(0) complex *(2)* in which five electron pair donors are coordinated to Co. This compound is formed on reaction of $Co_2(CO)_8$ with *(1)*[1,2] in toluene.



(1) *(2)*

Compound *(2)* crystallizes from ether/dichloroethane as dark green column shaped crystals displaying pronounced dichroism in transmitted light. They are air-stable; in solution they decompose slowly to form a red compound which has yet to be characterized.

If the five electron pair donors *(2)* were bound according to the usual rules of complex chemistry then the valence shell of the Co would contain one electron more than the krypton shell. Such a state should not be stable. No distinction is possible on the basis of spectroscopic and ESCA measurements. We have therefore subjected the compound to X-ray structure analysis.

Compound *(2)* crystallizes in the centrosymmetric space group Pnam with $a = 16.76(1)$, $b = 7.871(6)$, $c = 21.24(1)$ Å and

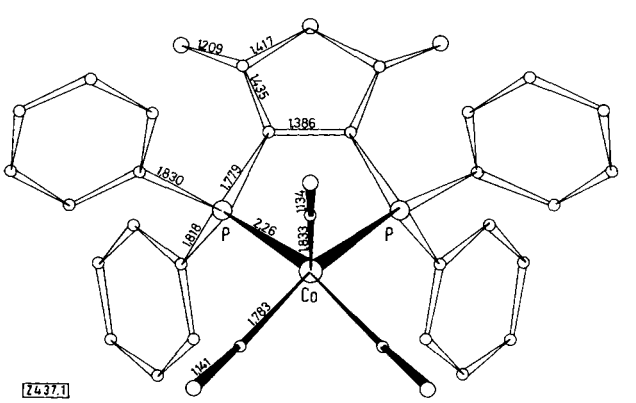


Fig. 1. Molecular structure of [bis(diphenylphosphino)maleic anhydride]tricarbonylcobalt(0) *(2)*. Viewed along the *b* axis.

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$Z=4$. The structure was solved for 1881 diffractometer data (320 of which were unobserved) by the heavy atom method and refined to an R value of 0.046 (Fig. 1).

The P atom of the chelated ligands *(1)* and the C atoms of the carbonyl groups form a distorted square pyramid with a plane of symmetry around the Co atom. The interatomic distances in the CO groups are very short, in accord with the position of the three ν(C≡O) vibrations observed between 2015 and 2075 cm^{-1} in the IR spectrum (KBr). The long C=C bond length in the phosphorus ligand indicates considerable delocalization of the π electrons. In a chelate complex formed by *(1)* and NiI_2 we have found the same C=C bond lengths as in *(2)* but C≡O lengths in the anhydride group which are 0.04 Å shorter than in *(2)*[2]. This difference in bonding is also manifested in the position of the two ν(C≡O) vibrations of the anhydride group which lie at 1840 and 1770 cm^{-1} in the NiI_2 complex of *(1)* but at 1740 and 1670 cm^{-1} in *(2)*.

The higher carbonyl vibration of the CO ligand which corresponds to that of the cationic complex $[Co(CO)_3[P(C_6H_5)_3]_2]^+$[3], and the lower carbonyl vibration of the anhydride group in *(2)* are regarded as indicating that the unpaired electron in *(2)* is delocalized over the phosphorus ligand. In the limiting state this becomes a radical anion, and the fivefold coordinated Co becomes a cation. The ESR signal[4] of this electron recorded in CH_2Cl_2 solution forms three groups of octets in the intensity ratio 1 : 2 : 1 corresponding to coupling of the electron with the phosphorus and the cobalt. The g factor and the coupling constants were found to be $g=2.00418$, $a_P=11.11$ G and $a_{Co}=1.21$ G. Magnetic measurements on the solid afforded $\mu_{eff}=2.10$ BM (at 25 °C). This value indicates a high orbital component of the magnetic moment.

[Bis(diphenylphosphino)maleic anhydride]tricarbonylcobalt(0) (2)

To a solution of $Co_2(CO)_8$ (2.56 g, 7.5 mmol) in toluene (20 ml) is added at 0 °C a solution of *(1)* (7.46 g, 16.0 mmol) in toluene (50 ml). Appearance of a green precipitate within a few minutes is accompanied by evolution of CO. After 30 min, filtration with exclusion of moisture affords *(2)* (8.60 g, 94 %).

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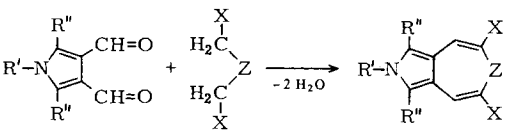
CAS Registry numbers:
(2), 58919-00-9; $Co_2(CO)_8$, 10210-68-1

[1] *D. Fenske* and *H. J. Becher*, Chem. Ber. *107*, 117 (1974); *108*, 2115 (1975).
[2] *H. J. Becher*, *W. Bensmann*, and *D. Fenske*, unpublished.
[3] *W. Hieber* and *W. Freyer*, Chem. Ber. *91*, 1230 (1958); *O. Vohler*, *ibid.* *91*, 1235 (1958).
[4] I am indebted to Dr. *Sustmann* for measurement and discussion of the ESR spectrum.

Synthesis of Thiepino[4,5-*c*]pyrrole Derivatives Having Sulfur in Different Oxidation States[1]

By *Richard Kreher*, *Helgard Möller*, and *Paul Heinz Wagner*[*]

Cyclizing condensation of pyrrole-3,4-dicarbaldehydes *(1)* with 1,2- or 1,3-bifunctional CH-acidic carbonyl compounds[2] is a versatile synthetic procedure for producing bicyclic hetarenes[3]. Its application to 1,3-bifunctional CH-acidic sulfur compounds *(2)* provides a facile entry to thiepino[4,5-*c*]pyrroles *(3)* having the sulfur atom in different oxidation states.



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

(a), Z = SO_2; *(b)*, Z = SO; *(c)*, Z = S; *(d)*, Z = $\overset{\oplus}{S}$–R

Table 1. Thiepino[4,5-*c*]pyrrole *S,S*-dioxides *(3a)*.

R′ = H, R″ = CH_3
(3aa), X = CO_2CH_3: yield 58 %, m.p. 300 °C (DMF/ethyl acetate).—*(3ab)*, X = $CO_2C_2H_5$: yield 63 %, m.p. 227—229 °C (DMF/ethyl acetate/ethanol).—*(3ac)*, X = C_6H_5—CO: yield 81 %, m.p. 260—264 °C (DMF/ethanol)
R′ = R″ = CH_3
(3ad), X = CO_2CH_3: yield 28 %, m.p. 242—244 °C (DMF/ethyl acetate).—*(3ae)*, X = $CO_2C_2H_5$: yield 75 %, m.p. 162—163 °C (ethanol).—*(3af)*, X = C_6H_5—CO: yield 92 %, m.p. 222—223 °C (ethanol).—*(3ag)*, X = *p*-Cl—C_6H_4—CO: yield 72 %, m.p. 299 °C (dec.) (acetonitrile/formamide).—*(3ah)*, X = *p*-CH_3O—C_6H_4—CO: yield 34 %, m.p. 224—226 °C (ethanol)

Table 2. Thiepino[4,5-*c*]pyrroles *(3c)*.

R′ = H, R″ = CH_3
(3ca), X = CN: yield 16 %, m.p. > 360 °C (ethanol).—*(3cb)*, X = C_6H_5—CO: yield 42 %, m.p. 240—242 °C (DMF/ethanol).—*(3cc)*, X = *p*-Cl—C_6H_4—CO: yield 84 %, m.p. 279—281 °C (ethanol).—*(3cd)*, X = *p*-CH_3O—C_6H_4—CO: yield 31 %, m.p. 265 °C (ethanol/ether)
R′ = R″ = CH_3 (all from ethanol)
(3ce), X = CN: yield 50 %, m.p. 308 °C.—*(3cf)*, X = C_6H_5—CO: yield 68 %, m.p. 210—212 °C.—*(3cg)*, X = *p*-Cl—C_6H_4—CO: yield 31 %, m.p. 238 °C.—*(3ch)*, X = *p*-Br—C_6H_4—CO: yield 58 %, m.p. 294 °C.—*(3ci)*, X = *p*-CH_3O—C_6H_4—CO: yield 82 %, m.p. 199 °C.—*(3cj)*, X = *p*-NO_2—C_6H_4—CO: yield 92 %, m.p. 310 °C (dec.)

In the presence of morpholine the dialdehydes *(1)* react smoothly with activated sulfonyl compounds *(2a)*, X = alkoxycarbonyl or aroyl, with elimination of water. The *S,S*-dioxide *(3a)*, R′ = R″ = CH_3, X = H, not directly accessible by this pathway can be obtained from the condensation product *(3ae)*, X = ethoxycarbonyl, by basic solvolysis and thermal decarboxylation (Table 1).

The sulfides *(2c)* can undergo condensation to give *(3c)* provided that the α-methylene groups are activated by cyano or aroyl groups; the effect of ester groups is inadequate in this case (Table 2).

Activation of the sulfide component *(2c)* can also be accomplished by *S*-alkylation. Cyclizing condensation of the sulfonium salts *(2d)* provides access to the heterocyclically conjugated sulfonium salts *(3d)*, which however are obtained in better yields from compounds *(3c)* by *S*-alkylation with trialkyloxonium tetrafluoroborates.

Synthesis of the *S*-oxides *(3b)* can be achieved by application of the same technique only if the sulfoxide component *(2b)* possesses sufficient thermal stability and chemical reactivity.

The structure of the thiepino[4,5-*c*]pyrroles *(3)* follows from their method of preparation and is confirmed by analytical and spectral data. The UV absorption maxima display a considerable structural dependence. A bathochromic shift of the long wave absorption maximum is seen to accompany the change in donor-acceptor properties of the hetero atom

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in the seven-membered ring: *(3a)*, $\lambda_{max}=375$ nm; *(3d)*, $\lambda_{max}=405$ nm; *(3c)*, $\lambda_{max}=575$ nm.

Compounds *(3)* are of interest mainly as sulfonyl or sulfur-homologous derivatives of isoindole. Representative reactivity studies have so far been performed with the readily accessible *S,S*-dioxides *(3a)*, X = alkoxycarbonyl, which fail to undergo cycloaddition reactions with activated dienophiles (dialkyl acetylenedicarboxylates, dialkyl azodicarboxylates) under the usual conditions.

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German version: Angew. Chem. *88*, 419 (1976)

CAS Registry numbers:
(1), R′=H, R″=CH_3, 56139-74-3; *(1)*, R′=R″=CH_3, 31618-55-0;
(2a), X=CO_2CH_3, 16002-30-5; *(2a)*, X=$CO_2C_2H_5$, 29771-87-7;
(2a), X=C_6H_5—CO, 3708-08-5; *(2a)*, X=*p*-Cl—C_6H_4—CO, 58881-54-2;
(2a), X=*p*-CH_3O—C_6H_4—CO, 58881-55-3; *(2c)*, X=CN, 5848-75-9;
(2c), X=C_6H_5—CO, 2461-80-5; *(2c)*, X=*p*-Cl—C_6H_4—CO, 23080-23-1;
(2c), X=*p*-CH_3O—C_6H_4—CO, 20177-84-8;
(2c), X=*p*-Br—C_6H_4—CO, 58881-56-4
(2c), X=*p*-NO_2—C_6H_4—CO, 58881-57-5;
(3aa), R′=H, R″=CH_3, 58881-58-6; *(3ab)*, R′=H, R″=CH_3, 58881-59-7;
(3ac), R′=H, R″=CH_3, 58881-60-0; *(3ad)*, R′=R″=CH_3, 58881-61-1;
(3ae), R′=R″=CH_3, 58881-62-2; *(3af)*, R′=R″=CH_3, 58881-63-3;
(3ag), R′=R″=CH_3, 58881-64-4;
(3ah), R′=R″=CH_3, 58881-65-5; *(3ca)*, R′=H, R″=CH_3, 58881-66-6;
(3cb), R′=H, R″=CH_3, 58881-67-7; *(3cc)*, R′=H, R″=CH_3, 58881-68-8;
(3cd), R′=H, R″=CH_3, 58881-69-9; *(3ce)*, R′=R″=CH_3, 58881-70-2;
(3cf), R′=R″=CH_3, 58881-71-3; *(3cg)*, R′=R″=CH_3, 58881-72-4;
(3ch), R′=R″=CH_3, 58881-73-5; *(3ci)*, R′=R″=CH_3, 58881-74-6;
(3cj), R′=R″=CH_3, 58881-75-7

[1] Structure and Reactivity of Isoannelated Heterocyclic Systems with $4n\pi$ and $(4n+2)\pi$ Electrons, Part 5.—This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.—Part 4: ref. [2a].

[2] a) *R. Kreher, G. Vogt*, and *M. L. Schultz*, Angew. Chem. *87*, 840 (1975); Angew. Chem. Int. Ed. Engl. *14*, 821 (1975); b) *R. Kreher* and *G. Vogt*, *ibid. 82*, 958 (1970) and *9*, 955 (1970), respectively.

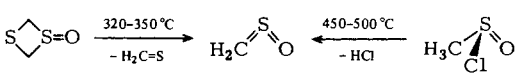
[3] Application of the synthetic principle: *M. J. Cook* and *E. J. Forbes*, Tetrahedron *24*, 4501 (1968); *M. Winn* and *F. G. Bordwell*, J. Org. Chem. *32*, 1610 (1967); *R. Guilard, P. Fournari*, and *M. Fontesse*, Bull. Soc. Chim. Fr. *1972*, 4349; literature cited under [3] and [4] in ref. [2a].

Photoelectron Spectrum of $H_2C{=}S{=}O$[1]

By *Eric Block, Hans Bock, Shamsher Mohmand, Pavel Rosmus*, and *Bahman Solouki*[*]

Dedicated to Professor Werner Schultheis

In contrast to other known thiocarbonyl *S*-oxides $R_2C{=}S{=}O$[2a], "sulfine" (thioformaldehyde *S*-oxide) $H_2C{=}S{=}O$, an isoelectronic derivative of sulfur dioxide, has so far defied all attempts at synthesis[2b]. The compound can however be generated as a short-lived species ($t_{1/2}\approx 30$—60 min) by pyrolysis of suitable starting materials; 1,3-dithietane 1-oxide[3] and, in particular, methanesulfinyl chloride[3,4] have proved to be suitable starting compounds for recording the photoelectron spectrum (Fig. 1).



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The PE spectra of the pyrolysis products (Fig. 1: b and c) contain the bands of thioformaldehyde $H_2C{=}S$[6] (b) and of hydrogen chloride (c).

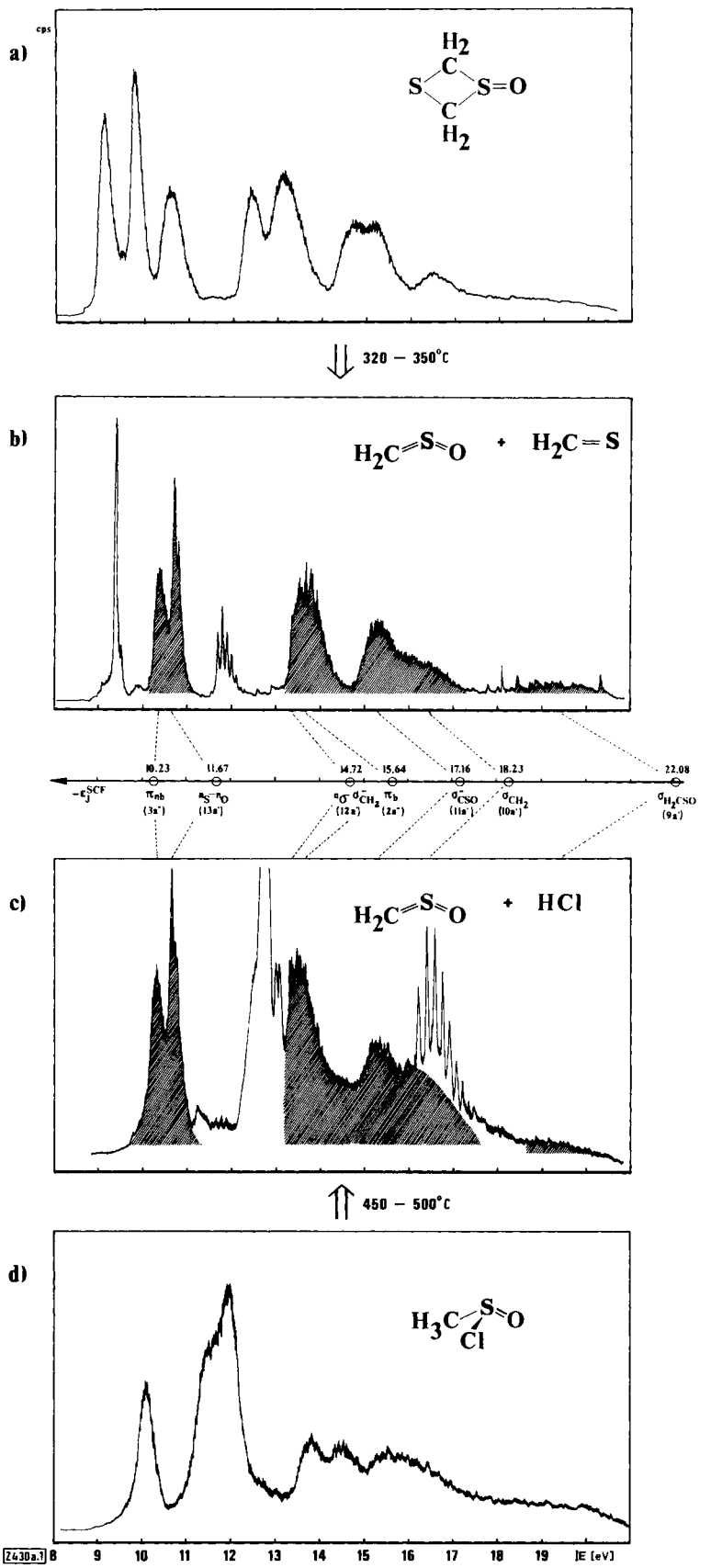
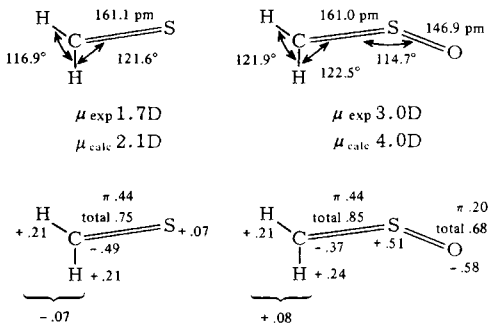


Fig. 1. [He(I)] PE spectra of 1,3-dithietane 1-oxide (a), methanesulfinyl chloride (d), and their pyrolysis products (a→b, d→c).

The hatched bands of "sulfine" can be deduced by comparison of the spectra (b) and (c). Their assignment follows from an *ab initio* SCF calculation[7] and by comparison with SSO and OSO[5]; it is supported by the resolved vibrational fine structures in the first three bands and by the change in the relative intensities in the [Ne] photoelectron spectrum[6b].

$H_2C{=}S{=}O$ can be regarded as the *S*-oxide of thioformaldehyde[6]; characteristic molecular data[3] and parameters[7] are:



As can be seen, the angle $\sphericalangle$ HCH is enlarged by incorporation of O; on the other hand the bond length $d_{C=S}$ remains unchanged. Population analysis indicates a redistribution of charge C→S→O; the $\pi_{C=S}$ bond remains constant. In comparison with other X=S=O derivatives the S=O bond is relatively weak—in accord with the experimentally observed[2] reductive elimination of O from thiocarbonyl *S*-oxides.

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CAS Registry numbers:
Thioformaldehyde *S*-oxide, 40100-16-1; thioformaldehyde, 865-36-1; 1,3-dithietane 1-oxide, 58816-63-0; methanesulfinyl chloride, 676-85-7

[1] Part 56 of Photoelectron Spectra and Molecular Properties.—Part 55: *H. Bock, E. Haselbach, E. Meyer*, and *H. Stafast*, Helv. Chim. Acta, in press.

[2] a) Cf., *e.g., G. Opitz*, Angew. Chem. *79*, 161 (1967); Angew. Chem. Int. Ed. Engl. *6*, 107 (1967); *B. Zwanenburg, L. Thijs, J. B. Broens*, and *J. Strating*, Q. Rep. Sulfur Chem. *5*, 79 (1970); *D. H. R. Barton et al.*, J. C. S. Chem. Commun. *1975*, 539, 557; and references cited therein.—b) Cf., *e.g., W. E. Truce* and *J. R. Norrel*, J. Am. Chem. Soc. *85*, 3231 (1963); *W. A. Sheppard* and *J. Diekmann*, *ibid. 86*, 1891 (1964); *S. Schürig*, Diplomarbeit, Universität Tübingen 1963.

[3] *E. Block, R. E. Penn, R. J. Olsen*, and *P. F. Sherwin*, J. Am. Chem. Soc. *98*, 1264 (1976); the microwave structure determination was performed by *R. E. Penn* and *R. J. Olsen*.

[4] Information due to *E. Block*. The pyrolysis apparatus is shown in ref. [5]. Cf. *S. Mohmand*, Diplomarbeit, Universität Frankfurt 1976.

[5] *H. Bock, B. Solouki, P. Rosmus*, and *R. Steudel*, Angew. Chem. *85*, 987 (1973); Angew. Chem. Int. Ed. Engl. *12*, 933 (1973); *P. Rosmus, P. Dacre, B. Solouki*, and *H. Bock*, Theor. Chim. Acta *35*, 129 (1974).

[6] a) *H. W. Kroto* and *R. J. Suffolk*, Chem. Phys. Lett. *15*, 545 (1972); b) *B. Solouki, S. Mohmand, P. Rosmus*, and *H. Bock*, unpublished; c) *P. J. Bruna, S. D. Peyerimhoff, R. J. Buenker*, and *P. Rosmus*, Chem. Phys. *3*, 35 (1974).

[7] Basis set: 10s/6p/1d for sulfur, 8s/4p for carbon and oxygen, 5s for hydrogen. $E_{total} = -1.391007 \times 10^4$ eV for the planar structure [3], $E_{total} = -1.390706 \times 10^4$ eV for conformation with twisted ($\omega = 90°$) CH_2 group.

Photoelectron Spectrum of HN=S=O[1]

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

The only photoelectron spectrum still required for a comparative discussion of bonding in the iso(valence)electronic molecules X=S=O (X = H_2C[1], HN, O[2], S[2]) was that of sulfinyl imide. Of the known methods of preparing[3,4] the compound, which polymerizes on condensation[5], we chose the reaction of Cl_2SO with NH_3 and were able to optimize the conditions with the aid of a PE spectrometer until the bands of the starting materials had largely disappeared (Fig. 1).

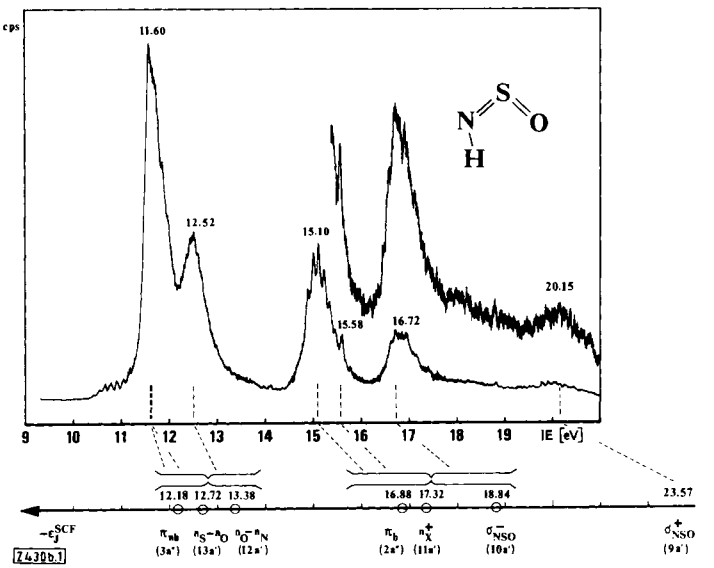

Fig. 1. [He(I)] PE spectrum of sulfinyl imide with assignment by an *ab initio* SCF calculation.

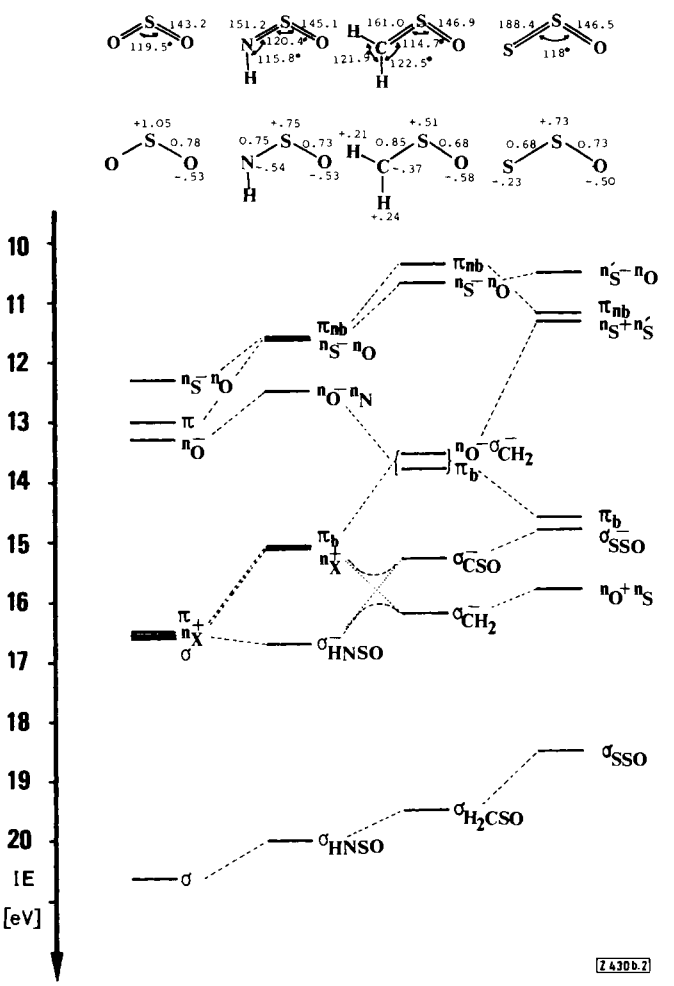

Fig. 2. Comparison of the X=S=O derivatives: ionization energies, characteristic molecular data (bond lengths in pm) and parameters.

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Assignment of the PE bands on the basis of an *ab initio* SCF calculation[6] is supported above all by comparison with OSO and SSO (Fig. 2): all X=S=O skeletons contain 18 valence electrons and—with the exception of $H_2C{=}S{=}O$—3 electron pairs in the plane of the molecule. Two separate regions with three ionizations each are expected according to *Walsh*[7] for such BAB or BAC systems and are indeed observed in all cases except H_2CSO (Figs. 1 and 2): on going from $HN{=}S{=}O$ to $H_2C{=}S{=}O$ the third ionization expectedly shows a sharp increase because the n_N electron pair is replaced by a σ_{CH} bond.

The comparison (Fig. 2) further reveals that the π ionizations π_{nb} and π_b run parallel to the calculated charges on the substituents X: $O > NH \approx S > CH_2$. The terminal oxygen in all derivatives XSO has a similar negative charge, thus leading to varying degrees of polarization in the remaining systems. The calculated bond populations decrease in the order $C{=}S > O{=}S \approx N{=}S > S{=}S$; the weakest S=O bond is found in $H_2C{=}S{=}O$[1].

The ionization energies and calculated quantities permit a better understanding of the properties of the molecules X=S=O: thus OSO proves to be the sole derivative stable under normal conditions; *cis*-HNSO is more stable than the *trans* isomer and is transformed, *inter alia*, into *cis*-NSOH upon irradiation in a matrix[5]; H_2CSO readily loses oxygen[8]; and SSO polymerizes *via* the polar S=S double bond[2].

Received: March 4, 1976 [Z 430b IE]
German version: Angew. Chem. *88*, 381 (1976)

CAS Registry number:
Sulfinyl imide, 13817-04-4

[1] Part 57 of Photoelectron Spectra and Molecular Properties.—Part 56: *E. Block, H. Bock, S. Mohmand, P. Rosmus,* and *B. Solouki*, Angew. Chem. *88*, 380 (1976); Angew. Chem. Int. Ed. Engl. *15*, 383 (1976).

[2] *H. Bock, B. Solouki, P. Rosmus,* and *R. Steudel*, Angew. Chem. *85*, 987 (1973); Angew. Chem. Int. Ed. Engl. *12*, 933 (1973); and references cited therein.

[3] *O. J. Scherer* and *R. Schmitt*, Chem. Ber. *101*, 3302 (1968); and references cited therein.

[4] *W. H. Kirchhoff*, J. Am. Chem. Soc. *91*, 2437 (1969). The apparatus built according to the cited paper by *P. W. Schenk*, Chem. Ber. *75*, 94 (1942), was connected directly to the PE spectrometer.

[5] *P. O. Tchir* and *R. D. Spratley*, Can. J. Chem. *53*, 2311, 2312, 2331 (1975).

[6] Basis set: 10s/6p/1d for S, 8s/4p for N and O, 5s for H. $E_{total}^{cis} = -1.434496 \times 10^4$ eV, $E_{total}^{trans} = -1.434476 \times 10^4$ eV.

[7] Cf. *P. Rosmus, P. Dacre, B. Solouki,* and *H. Bock*, Theor. Chim. Acta *35*, 129 (1974); references cited therein.

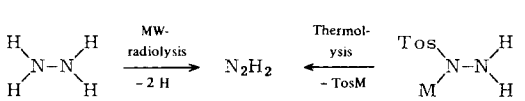
[8] *E. Block, R. E. Penn, R. J. Olsen,* and *P. F. Sherwin*, J. Am. Chem. Soc. *98*, 1264 (1976).

The Existence of Isomeric Diazenes (Diimines)[1]

By *Nils Wiberg, Gerd Fischer,* and *Heinz Bachhuber*[*]

Dedicated to Professor Egon Wiberg on the occasion of his 75th birthday

Two methods have hitherto become available for the preparation of *gaseous* diazene (diimine)[4], namely microwave radiolysis of hydrazine[2] and thermolysis of alkali metal tosylhydrazides[3] (for preparation of *dissolved* diazene, cf. ref.[5]).



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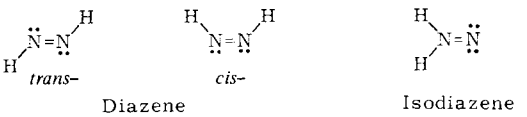
The N_2H_2 produced from the lithium salt by the second method and purified from the co-products nitrogen and and hydrazine can be deposited as lustrous yellow *solid* diazene on surfaces cooled by liquid nitrogen[3]. In contrast, the N_2H_2 produced by the first method cannot be separated from the co-product ammonia (and other nitrogen hydrides) and can only be condensed together with large quantities of NH_3[2, 6a].

Three possible constitutional or configurational isomers can be envisioned for "diazene":



IR data show the N_2H_2 arising from lithium tosylhydrazide and examined in the solid state at −196 °C to be *trans*-diazene[3]. We have now found, however, that the N_2H_2 produced in the same way from cesium tosylhydrazide, which contains hardly any by-products, differs in its physical and chemical properties from *trans*-diazene, thus indicating formation of an isomer (*cis*-diazene or isodiazene). Thus the intensity ratio of the mass peaks due to the molecular and fragment ions $N_2H_2^+$, N_2H^+, and N_2^+ (18 eV) is 100:32:1 (*trans*-diazene) and 100:46:5 (new isomer). Striking differences are also noted in the ionization and appearance energies of the ions $N_2H_2^+$ and N_2H^+ as determined under strictly comparable conditions for the two diazenes by the RPD method[7a] (cf. Fig. 1)[7b]. Ionization leading to the same fragment N_2H^+ requires 0.56 ± 0.1 eV/molecule more energy in the case of *trans*-diazene than in the case of the isomeric species; thus the latter form has an energy content some 13 kcal/mol (= 54 kJ/mol) greater than that of the former.

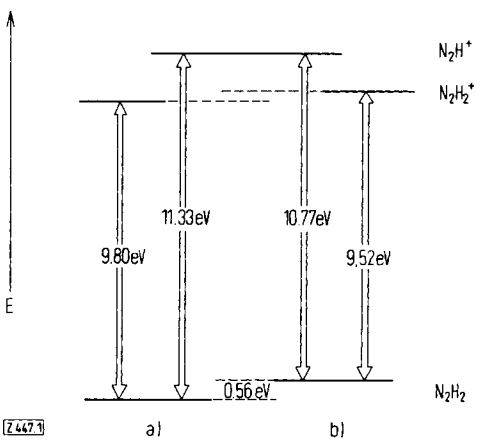


Fig. 1. Energies determined by electron impact (error: ±0.05 eV) for the transitions $N_2H_2 \rightarrow N_2H_2^+ + e$ and $N_2H_2 \rightarrow N_2H^+ + H + e$. The diimine was produced by thermolysis from a) lithium tosylhydrazide (*trans*-diazene) and b) cesium tosylhydrazide (isomeric diazene).

Unlike the yellow *trans*-diazene ($\lambda_{max} = 386$ nm) this isomer ($\lambda_{max} \approx 260$ nm) cannot be deposited without partial decomposition on surfaces cooled by liq. N_2. It also displays a greater reactivity towards ammonia, with which it is shown by IR studies to form a yellow addition compound ($\lambda_{max} = 398$ nm) of unknown structure. The same adduct is also formed from *trans*-diazene and ammonia; however, the reaction requires several hours at 110 K with *trans*-diazene but only a few minutes at 72 K in the case of the isomeric diazene. Hence at 77 K (liquid nitrogen) *trans*-diazene/ammonia are deposited as a co-condensate, but isomeric diazene/ammonia as an adduct.

The N_2H_2 produced together with much ammonia by microwave radiolysis of hydrazine corresponds in its properties to the thermolysis product of cesium tosylhydrazide. The absorption bands of the N_2H_2/NH_3 condensate observed alongside those of ammonia in the IR spectrum recorded at 77 K are not due to *trans*-diazene, as formerly proposed[6], but instead to the adduct immediately formed from the isomeric diazene and ammonia under such conditions[8].

Since its instability has so far precluded recording of a low-temperature IR spectrum of pure "isomeric diazene", its structure still remains open. On account of the relatively large energy difference of the two forms of N_2H_2 (quantum mechanical[9] and chemical considerations indicate similar energy contents for *cis*- and *trans*-diazene) we tentatively prefer the isodiazene over the *cis*-diazene structure for the new isomer. Moreover, the fact that this species can be passed unchanged through several meters of glass tubing without isomerization at low pressures and in the absence of catalysts would also suggest that it is isodiazene. According to the Woodward-Hoffmann rules for the conservation of orbital symmetry, isodiazene, in contrast to *cis*-diazene, cannot readily rearrange to *trans*-diazene; in the presence of catalysts (*e.g.* gaseous hydrogen chloride), however, the expected transformation of the more energetic form into the thermodynamically more stable *trans*-diazene is observed.

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German version: Angew. Chem. *88*, 386 (1976)

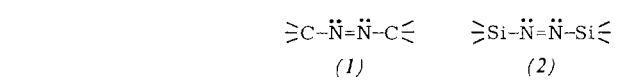
CAS Registry numbers:
trans-Diazene, 15626-43-4; isodiazene, 28647-38-3

[1] Part 21 of Diimine and Its Derivatives.—Part 20: *N. Wiberg, H. W. Häring*, and *O. Schieda*, Angew. Chem. *88*, 383 (1976); Angew. Chem. Int. Ed. Engl. *15*, 386 (1976).
[2] *S. N. Foner* and *R. L. Hudson*, J. Chem. Phys. *28*, 719 (1958).
[3] *N. Wiberg, H. Bachhuber*, and *G. Fischer*, Angew. Chem. *84*, 889 (1972); Angew. Chem. Int. Ed. Engl. *11*, 829 (1972); Chem. Ber. *107*, 1456 (1974).
[4] Another synthetic pathway to N_2H_2 has meanwhile been discovered in the thermolysis of triazanium sulfate ($N_3H_7SO_4$) [*N. Wiberg* and *P. Wanninger*, unpublished].
[5] *S. Hünig, H. R. Müller*, and *W. Thier*, Angew. Chem. *77*, 368 (1965); Angew. Chem. Int. Ed. Engl. *4*, 271 (1965).
[6] a) *A. Trombetti*, J. Chem. Soc. *A 1971*, 1086; b) *V. E. Bondybey* and *I. W. Nibler*, J. Chem. Phys. *58*, 2125 (1973).
[7] a) *R. E. Fox, W. M. Hickam, D. H. Grove*, and *T. Kjeldaas*, Rev. Sci. Instrum. *26*, 1101 (1955).—b) Concerning N_2H_2 ionization and appearance energies so far determined, cf. refs. [2, 3] and *G. Holzmann* and *R. Minkwitz*, Z. Anorg. Allg. Chem. *413*, 72 (1975); *C. Willis, F. P. Lossing*, and *R. A. Back*, Can. J. Chem. *54*, 1 (1976).
[8] Whereas pure *trans*-diazene decomposes above −180°C, the adduct decomposes only above about −130°C. In the presence of excess ammonia it can even be evaporated to a NH_3/N_2H_2 gas mixture with partial thermolysis by rapid warming; N_2H_2 can be detected for several minutes in this mixture [cf. *C. Willis* and *R. A. Back*, Can. J. Chem. *51*, 3605 (1973)].
[9] *E. R. Talaty, A. K. Schwartz*, and *G. Simons*, J. Am. Chem. Soc. *97*, 972 (1975), and references cited therein.

Bis(trimethylsilyl)diazene as a Complex Ligand[1]

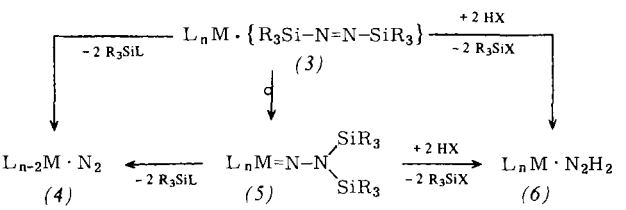
By *Nils Wiberg, H. W. Häring*, and *Oswald Schieda*[*]

Bis(organyl)diazenes (organic azo compounds) having the characteristic atomic grouping *(1)* can coordinate to subgroup metals either *via* their free n-electron pairs to form σ-complexes or *via* their π-electron pair to give π-complexes[2]. Owing to the extremely high and low energy, respectively, of their highest occupied n- and lowest unoccupied π*-molecular orbital[3] relative to those of *(1)*, bis(silyl)diazenes *(2)* should be even more suitable as σ- and π-complex ligands (scope for forming strong bonds with the "basic" n-electron pairs and strong back-bonds with the "acidic" π*-electron vacancy).



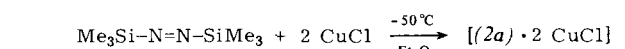
(1) *(2)*

Coordination compounds of azosilanes of general type *(3)* attract particular interest on account of the "chemical mobility" of the substituents on the azo group (R_3Si) which is absent in complexes of organic azo compounds. Thus the complexes *(3)* should undergo R_3SiL elimination, R_3Si rearrangement, and protolysis of Si—N bonds according to



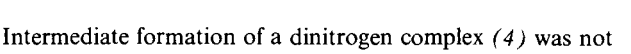
to form dinitrogen complexes *(4)*, silylated isodiazene complexes *(5)*[4a], and desilylated diazene complexes *(6)*[4b], respectively. Some impression of the problems involved is given by the reactions of bis(trimethylsilyl)diazene *(2a)* with copper(I) chloride and with bis(cyclopentadienyl)vanadium.

Like organic azo compounds, *(2a)* reacts with copper(I) chloride according to



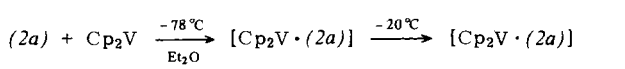
(2a)

at low temperatures to form a crystalline reddish brown 1:2 adduct[5] which is insoluble in ether; the two CuCl units are probably bonded by way of the two n-electron pairs of *(2a)* as in the case of the corresponding azomethane complex[6] (formation of a *σ-diazene complex*). Above −30°C the dinuclear azosilane complex decomposes with elimination of Me_3SiCl and liberation of nitrogen:



Intermediate formation of a dinitrogen complex *(4)* was not observed. The azosilane complex is not attacked by methanol below −30°C; the silyl groups cannot be removed by protolysis.

At −78°C *(2a)* reacts smoothly with bis(cyclopentadienyl)-vanadium, which yields a π-complex with azobenzene[7], to form a blackish green complex which transforms into a dark reddish brown paramagnetic complex at −20°C, which is stable up to at least 100°C and can therefore be vacuum sublimed at 60°C[8].



black-green dark red-brown

As shown by X-ray structure analysis[9] the ligand *(2a)* is present in the iso-form in the reddish brown complex (formation of an *isodiazene complex*). Apparently Cp_2V initially forms a "normal" complex $Cp_2V \cdot Me_3SiNNSiMe_3$ with *(2a)* (formation of a *π-diazene complex*?) which rearranges to the thermodynamically more favorable isomer $Cp_2V{=}NN(SiMe_3)_2$.

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The action of methanol on the reddish brown compound does not lead to liberation of trimethylsilyl groups but instead, according to

$$2\ Cp_2VNN(SiMe_3)_2 \xrightarrow[-2\ CpH]{+2\ MeOH} [Cp(MeO)VNN(SiMe_3)_2]_2$$

to loss of cyclopentadienyl groups with formation of a brown diamagnetic complex of unknown structure which can be vacuum sublimed at 110°C. Its ^{1}H-NMR spectrum contains only one signal for the trimethylsilyl protons and one for the methoxy protons at $\delta = -22$ and -128 Hz (TMS internal standard, C_6H_6) respectively. The course of reaction can be interpreted by assuming that the vanadium central atom, which formally possesses an "excess" electron (*i.e.* 19 valence electrons)[10] in the complex $Cp_2VNN(SiMe_3)_2$, confers negative partial charges upon the two Cp ligands, thus facilitating attack of the cyclopentadienyl ring by a proton.

Procedure:

A mixture of CuCl (10.1 mmol) and $(Me_3Si)_2N_2$[3] in diethyl ether (50 ml) is stirred with exclusion of oxygen and moisture at −50°C until all the CuCl has dissolved (*ca.* 3 h). During this process, the initially yellow, then reddish brown, and finally colorless solution precipitates reddish brown fine crystals of [*(2a)*·2 CuCl], which is purified by repeated washing with ether.

Combination of Cp_2V (5.0 mmol) in diethyl ether (25 ml) at −78°C with $(Me_3Si)_2N_2$[3] in ether (10 ml) under similar conditions immediately yields a dark green solution which deposits blackish green crystals on concentration. Above −20°C they transform into the dark brown ismeric product $Cp_2V{=}NN(SiMe_3)_2$, m.p. 76—78°C, which can be recrystallized from ether.

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CAS Registry numbers:
[*(2a)*·2 CuCl], 59301-73-4; $Cp_2V\cdot\{Me_3SiNNSiMe_3\}$, 59301-74-5; $Cp_2V{=}NN(SiMe_3)_2$, 59301-87-0; Cp_2V, 1277-47-0; Cp_2TiCl_2, 1271-19-8; $[Cp(MeO)VNN(SiMe_3)_2]_2$, 59361-81-6

[1] Part 20 of Diimine and Its Derivatives. Also Part 38 of Compounds of Silicon and Its Group Homologs. This work was supported by the Deutsche Forschungsgemeinschaft.—Parts 19 and 37, respectively: *N. Wiberg, S. K. Vasisht*, and *G. Fischer*, Angew. Chem. *88*, 257 (1976); Angew. Chem. Int. Ed. Engl. *15*, 236 (1976).

[2] Cf., *e.g., M. Herberhold, W. Golla*, and *K. Leonhard*, Chem. Ber. *107*, 3209 (1974); references cited therein.

[3] *N. Wiberg, W.-Ch. Joo*, and *W. Uhlenbrock*, Angew. Chem. *80*, 661 (1968); Angew. Chem. Int. Ed. Engl. *7*, 640 (1968); *N. Wiberg, ibid. 83*, 379 (1971) and *10*, 374 (1971), respectively.

[4] Complexes of isodiazene N=NH$_2$ and diazene HN=NH are already known: a) *J. Chatt*, J. Organomet. Chem. *100*, 17 (1975); b) *D. Sellmann, A. Brandl*, and *R. Endell, ibid. 90*, 309 (1975).

[5] Corresponding compounds showing somewhat greater thermal stability are obtained with CuBr and CuI.

[6] *I. D. Brown* and *J. D. Dunitz*, Acta Crystallogr. *13*, 28 (1960).

[7] *G. Fachinetti, G. Fochi*, and *C. Floriani*, J. Organomet. Chem. *57*, C 51 (1973).

[8] According to

$$Cp_2TiCl_2 + 2\ (2a) \rightarrow [Cp_2Ti\cdot(2a)] + N_2 + 2\ Me_3SiCl$$

and

$$Cp_2TiCl_2 + (Me_3Si)_2N_2Li_2 \rightarrow [Cp_2Ti\cdot(2a)] + 2\ LiCl$$

a dark violet diamagnetic titanium complex, which is sublimable at 60°C, is also accessible. Its ^{1}H-NMR spectrum contains only a single trimethylsilyl proton signal at $\delta = -17.5$ Hz (TMS int. std., Et_2O). It probably has the structure $Cp_2TiNN(SiMe_3)_2$ analogous to $Cp_2VNN(SiMe_3)_2$.

[9] *M. Veith*, Angew. Chem. *88*, 384 (1976); Angew. Chem. Int. Ed. Engl. *15*, 387 (1976).

[10] $(Me_3Si)_2N{=}\ddot{N}$ can act as a four-electron donor.

Structure of an "Isodiimine" Complex: Bis-(trimethylsilyl)isodiazenebis(cyclopentadienyl)vanadium

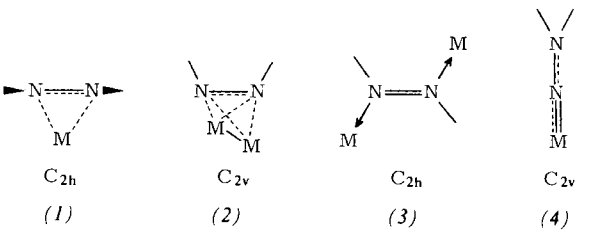
By *Michael Veith*[*]

Complexes of diazene (diimine) derivatives with transition metals can be distinguished according to structural criteria:

1) The azo group froms a π bond to the metal, the substituents on the NN unit being *trans* configurated (type *(1)*). In the case of dinuclear complexes the diazene group spans the coordination centers in such a way that the two metal atoms and the two nitrogen atoms approximately form a tetrahedron (type *(2)*). In both structural types the N—N bond length is considerably greater than in the free molecule and almost reaches the value for a single bond (137—139 pm)[1].

2) The azo group is coordinated to the metal *via* a σ bond (type *(3)*). The N—N bond length is hardly affected (125—126 pm). In this way diazenes usually act as bridging ligands between two metal atoms[2].

3) The substituents on the azo group migrate during complex formation and the resulting 1,2-disubstituted diazene ligand coordinates *via* a multiple bond between the terminal nitrogen and the metal atom (type *(4)*).



The last-named structural type is assumed for the N_2H_2 ligand in the cation of $[W(N_2H_2)Cl(diphos)_2]BPh_4$. Although the positions of the hydrogen atoms could unfortunately not be established on X-ray structure analysis, the N—N bond length of 137 pm, the WNN angle of 171°, and the short W—N distance of 173 pm do evidence a structure of type *(4)*.

In this communication we wish to report the results of a structure determination[4] performed on a complex formed

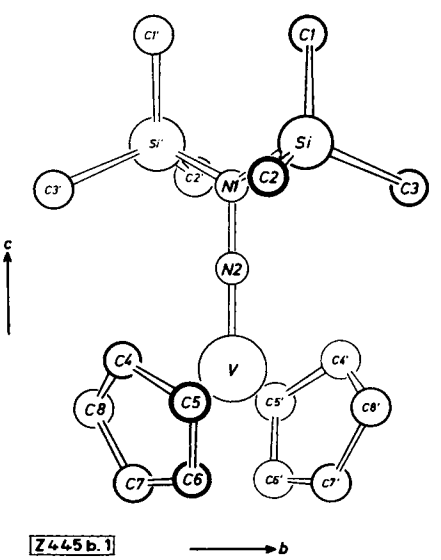


Fig. 1. Molecular structure of bis(trimethylsilyl)isodiazenebis(cyclopentadienyl)vanadium

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Selected bond lengths [pm] and angles [°]:

V—N(2)	166.6(6)	Si—C	184(1)	(average value)
N(1)—N(2)	136.9(9)	V—C	240(13)	(average value)
Si—N(1)	175.6(3)			
∢VN(1)N(2)	180	∢SiN(1)Si'	136.7(4)	

by reaction of bis(trimethylsilyl)diazene with bis(cyclopentadienyl)vanadium[5]. The structure of this complex (Fig. 1) provides the first insight into the geometry of a monohaptocoordinated isodiazene.

In the crystal the molecule strictly possesses C_2 symmetry, although deviations from C_{2v} symmetry are only minimal. The V, N(1), and N(2) atoms are located on the twofold axis, *i.e.* in a linear arrangement. The entire isodiazene ligand is strictly planar, a feature which should facilitate delocalization of π electrons from vanadium across to silicon. Other features of the molecular structure are:

1) The V—N bond length is exceptionally short. A metal-nitrogen multiple bond is present, as is also encountered in Cl_3VNCl (V—N, 164.2 pm[6]).

2) The N—N bond length is considerably greater than in free bis(trimethylsilyl)diazene (117.1(7) pm) and thus almost lies in the range of the N—N single bond[7].

3) The mutual eclipsed arrangement of the trimethylsilyl groups is associated with a significant opening of the SiN(1)Si' angle. The SiNSi angle in bis(dioxane)potassium bis(trimethylsilyl)amide[8]—a compound which also has an eclipsed conformation of the Me_3Si groups—amounts to 136.2°.

4) The cyclopentadienyl ligands display a distinct tendency to engage in trihapto rather than the usual pentahapto coordination. Thus the vanadium-carbon distances for C(4), C(5), and C(8) are 20 pm shorter than those for C(6) and C(7). For the same reason the cyclopentadienyl ring is not strictly planar, but is made up of a triangle [C(4), C(5), C(8)] and a planar rectangle [C(5), C(6), C(7), C(8)] whose normals enclose an angle of 6.2°. The deviation from planarity of the five-membered ring is thus directed away from the metal atom.

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CAS Registry number:
Bis(trimethylsilyl)isodiazenebis(cyclopentadienyl)vanadium, 59301-87-0

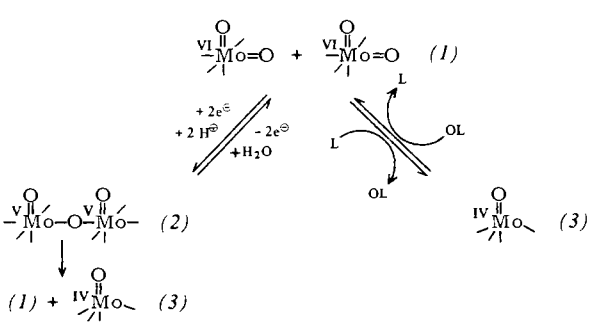
[1] *R. S. Dickson, J. A. Ibers, S. Otsuka,* and *Y. Tatsuno*, J. Am. Chem. Soc. *93*, 4636 (1971); *R. J. Doedens* and *J. A. Ibers*, Inorg. Chem. *8*, 2709 (1969).
[2] *K. K. Kakati* and *B. Chaudhuri*, Acta Crystallogr. *B24*, 1645 (1968); *G. Huttner, W. Gartzke,* and *K. Allinger*, J. Organomet. Chem. *91*, 47 (1975).
[3] *G. A. Heath, R. Mason,* and *K. M. Thomas*, J. Am. Chem. Soc. *96*, 259 (1974).
[4] X-Ray diffraction, single crystal (Picker four-circle diffractometer). Space group Fdd2; cell constants $a=1692(1)$, $b=2140(1)$, $c=1105.3(7)$ pm; $Z=8$. 1056 reflections, R value = 4.6 %.
[5] *N. Wiberg, H. W. Häring,* and *O. Schieda*, Angew. Chem. *88*, 383 (1976); Angew. Chem. Int. Ed. Engl. *15*, 386 (1976).
[6] *J. Strähle* and *H. Bäringhausen*, Z. Anorg. Allg. Chem. *357*, 325 (1968).
[7] *M. Veith* and *H. Bärnighausen*, Acta Crystallogr. *B30*, 1806 (1974); *M. Veith, ibid. B31*, 678 (1975).
[8] *A. M. Domingos* and *G. M. Sheldrick*, Acta Crystallogr. *B30*, 517 (1974).

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

The reaction mechanism of enzymes containing molybdenum is reviewed by *R. A. D. Wentworth*. The most important enzymes containing Mo catalyze reductions of dinitrogen to ammonia, nitrate to nitrite, and oxidations of sulfite to sulfate, xanthine to uric acid, and aldehydes to carboxylic acids. A discussion of the chemistry of inorganic oxo complexes of Mo^{VI}, Mo^{V}, and Mo^{IV} leads to a new suggestion for the mechanism of oxidase and reductase action:



In its resting state, the enzyme contains two hexacoordinate Mo^{VI} atoms carrying at least two oxo ligands *(1)*. Under physiological conditions these can be reduced to a dinuclear Mo^{V} species *(2)*; *(2)* can disproportionate to a pentacoordinate Mo^{IV} species *(3)* and *(1)*. Species *(3)* is the active entity effecting reduction by taking over an oxo ligand from OL, the oxidized form of the substrate (reductase action). Acting as oxidase, *(1)* loses an oxo ligand to L, the reduced substrate, and forms *(3)*. This mechanism is also able to explain the inhibition of xanthine oxidase by allopurinol. [Mechanisms for the Reactions of Molybdenum in Enzymes. Coord. Chem. Rev. *18*, 1—27 (1976); 136 references]

[Rd 849 IE—H]

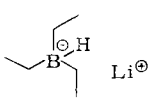
The evolution of bacterial energy metabolism is discussed by *R. E. Dickerson, R. Timkovich,* and *R. J. Almassy* on the basis of the folding of the evolutionarily homologous cytochromes of type c. Oxygen respiration of bacteria and eukaryotes is considered to have developed from a double purpose (photosynthesis and respiration) electron transport chain, as found in the purple non-sulfur bacteria, with loss of photosynthetic capability. An elaborate scheme is drawn up for the development of photosynthesis and respiration in bacteria, beginning with a symbiotic sulfur cycle, followed by development of the Krebs cycle, and culminating in the present symbiotic oxygen cycle between plants and animals. [The Cytochrome Fold and the Evolution of Bacterial Energy Metabolism. J. Mol. Biol. *100*, 173—491 (1976); 42 references]

[Rd 852 IE—R]

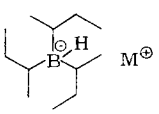
NMR and the periodic system is the theme of a review by *R. K. Harris*. The author does not deal with ^{1}H-, ^{11}B-, ^{13}C-, ^{19}F-, and ^{31}P-NMR spectroscopy, but with the possibility of using more unusual nuclei in NMR studies. Suitable nuclei are those (like ^{1}H, ^{19}F, and ^{31}P) which have spin quantum number $I = 1/2$, which occur in *ca.* 100% natural purity, and which have a relatively high magnetic moment. Apart from the above mentioned nuclei only ^{89}Y, ^{103}Rh, and ^{169}Tm can fulfill these three conditions. But if nuclei with $I > 1/2$ or natural purity $< 100\%$ are also considered, there is at least one nucleus that comes into question in each group of the periodic system. [NMR and the Periodic Table. Chem. Soc. Rev. 5, 1—22 (1976); 81 references]

[Rd 854 IE—F]

Selective reductions with complex hydrides are discussed by *E. R. H. Walker*. $NaBH_4$ and $LiAlH_4$ are universal reducing agents, but their selectivity leaves much to be desired. The author illustrates how the properties of the two reagents alter on changing the solvent, the cation, or replacing some of the hydrogen atoms. For example, $LiBH_4$ can reduce esters and is thus a stronger reducing agent than $NaBH_4$. The derivative $LiBEt_3H$ ("superhydride") *(1)* is an extremely nucleophilic compound which rapidly reduces alkyl halides, but not aryl halides. Compound *(2)*, M = Li or K, permits selective reductions. Alkoxy-substituted $LiAlH_4$, *e.g.* lithium tris(*tert*-butoxy)-hydridoaluminate is a mild reducing agent which selectively reduces acid chlorides to aldehydes. "RED-AL" *(3)* has practically the same reducing action as $LiAlH_4$, but cannot be handled safely and conveniently. [The Functional Group Selectivity of Complex Hydride Reducing Agents. Chem. Soc. Rev. 5, 23—50 (1976); 64 references]



(1)



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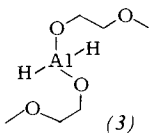

(3)

[Rd 855 IE—F]

Advances in thin-layer chromatography, particularly in direct combination with thermal procedures, are reviewed in an article by *E. Stahl*. Since the preparation of the sample is often more time-consuming than the actual analysis attempts have been made to develop "on-line" methods. In the simplest case a metal block with a hole bored in it to hold sample and container is used. The metal block is either preheated or heated according to a temperature program; if necessary, volatile components are fed onto a moving DC plate. [Advances in the Field of Thermal Procedures in Direct Combination with Thin-Layer Chromatography. Acc. Chem. Res. 9, 75—80 (1976); 42 references]

[Rd 857 IE—L]

BOOK REVIEWS

Statistische Versuchsplanung (Statistical Planning of Experiments). By *G. Retzlaff, G. Rust*, and *J. Waibel*. Verlag Chemie, GmbH, Weinheim 1975. 1st Edit., ix, 211 pp., 52 figs., 52 tables, bound DM 58.—.

The aim of every experimenter is to make his object capable of visualization by physical concepts and if possible quantifiable by physical models. If, however, at the beginning of the investigation there is no physical representation, if the problem becomes very complex because of the many interfering factors and in addition the measurements are subject to considerable errors, or if a certain goal must be reached rapidly and without taking such considerations into account, then statistical planning of the experiment may be useful. The literature on this subject has so far suffered the disadvantage that it is written either in English or in a mathematical abstract form that is difficult for the chemist. The strength of the present book is that, right at the beginning, in about 40 pages, the technique of factorial experiment planning is explained in easily understandable form. Anyone who then has no wish to probe further will still know enough to be able, if necessary, to call in an expert. It is not quite clear why the authors failed to include the process of the steepest gradient (Box-Wilson method) and a suitable example. In the following two chapters the basic statistics (Chapter 3) are treated so far as is necessary for consideration of the error in factorial experiment planning (Chapter 4). Anyone with experience of the halfnormal plot will probably regret that this method is mentioned only in a footnote.

Not all the subsequent chapters will interest the experimental chemist to the same extent. Reference should, however, be made to the chapter on regression calculation (Chapter 7) and the simplex method (in Chapter 9). Summarizing, it can be said that this book can be thoroughly recommended to anyone who has to do with the planning and evaluation of experiments.

Otto Wörz [NB 309 IE]

Transport Phenomena. By *W. J. Beek* and *K. M. K. Muttzall*. John Wiley & Sons. Ltd., London—New York 1975. 1st edit., x, 298 pp., numerous figs. and tables, bound, £ 9.85.

This book is based on a series of lectures. In four chapters it covers the fundamental laws of the transport of momentum, heat, and mass and demonstrates their importance by numerous important examples from process technology.

Following the formulation of the conservation laws in Chapter 1, the principles of flow theory and dimensional analysis are discussed in Chapter 2, and these are then used to work through a large number of important problems (*e.g.* the pressure loss in pipelines of various geometrical shapes, flow measurement, flow through solid beds, fluidized beds, and residence-time distribution). Chapter 3 begins with a discussion of stationary and nonstationary heat conduction, the treatment including questions of heat transfer and heat transmission as well as various types of heat exchangers and problems of heat transfer during boiling and condensation.

In the last chapter the laws of material transport are discussed, covering not merely stationary and nonstationary diffusion but also continuous material exchange in two-phase flows and the influence of diffusion on conversion in homogeneous and heterogeneous reactions.

The book is impressive in the wealth of material offered, this being skilfully assembled so that, in conjunction with exercises tied to the text, it demands the reader's active participation. Since working through the text does not require sophisticated mathematical knowledge, the book can be highly recommended as a course book alongside lectures on the

fundamentals of industrial processes. The many examples that keep close to practice, treated by means of numerous tables and diagrams, also provide stimulation and help to the practising professional.

Diethard Hesse [NB 314 IE]

Einführung in die Theoretische Chemie. Band 1: Quantenmechanische Grundlagen. (Introduction to Theoretical Chemistry. Vol. 1: Quantum-Mechanical Principles.) By *W. Kutzelnigg*. Verlag Chemie, GmbH, Weinheim 1975. 1st edit., xxiii, 297 pp., 23 figs., 9 tables, cloth, DM 68.—.

It is general experience that familiarization with the principles of quantum mechanics proves particularly difficult for the chemist. Very closely connected with this is the usually uncritical, positive or negative, attitude adopted towards the numerical results of quantum-mechanical investigations, which are published today in such large numbers. In this book the author tries to play a mediating role; building on the smallest possible number of mathematical assumptions, he acquaints the reader progressively with the basic formalism and the most important methods and results of quantum mechanics. The approach has indeed been highly successful. Mathematical formulations going beyond the basic facts of differential and integral calculus, with which almost every student of chemistry is nowadays familiar, are given in the Appendix. A very commendable feature is that the author has made it a definite policy not to try to dodge difficulties. Knowledge that the reader does not already possess must be acquired during the study of each successive chapter. Accordingly, for those with little previous knowledge the book will undoubtedly be rather difficult reading.

Some may regard the author's concept of the extent of theoretical chemistry as rather too narrow. According to the list of contents, the second volume will provide a review of the theory of the chemical bond, the various methods of quantum chemistry, and the results of numerical calculations. The present volume is already directed to this end. The author quite consciously left aside anything that was not immediately relevant to his purpose. Time-dependent phenomena such as scattering processes and molecular collisions theory, tunneling phenomena, and theoretical attempts to describe chemical processes, as well as conditions in the energy continuum and relativistic effects are not considered. The numerically evaluable approximation methods for the solution of the Schrödinger equation are naturally treated in great detail.

After a brief section on the basic principles of classical mechanics essential for a description of atoms and molecules, the postulates of quantum mechanics are presented and some simple examples of exactly soluble Schrödinger equations are discussed. Here it should be emphasized that the author is always at pains to find the didactically most favorable formulation. For example, the eigenstates of a harmonic oscillator are derived with the aid of creation and annihilation operators, whereas in other cases conventional methods are preferred for the solution of differential equations. Several sections are devoted to angular momentum operators and their properties and to the hydrogen atom. Two further chapters treat the most important approximation methods of quantum mechanics, variational calculus and perturbation theory. The remaining six sections present a comprehensive theory of atoms that, starting from elementary models, leads up to problems of spin-orbit coupling and electron correlation effects.

Summarizing, this book can be described as an introduction, designed for chemists and eminently successful, to the fundamentals of quantum mechanics. Put together with great skill, the presentation moves in general along the conventional lines of textbooks in this field. It must be specially emphasized that the author really has succeeded in building on a very modest mathematical foundation, gradually leading the reader up to more difficult formalism. Account is taken of the latest developments in quantum chemistry by devoting great attention to the concepts needed for a deeper understanding of numerical methods of calculation. The book can be warmly recommended both to advanced students of chemistry and to trained chemists who wish to learn the fundamental facts of quantum mechanics and their applications in chemistry.

Peter Schuster [NB 317 IE]

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Elementary Processes at Gas/Metal Interfaces[**]

By Gerhard Ertl[*]

Recent years have seen the development of several physical methods for the study of solid surfaces under ultrahigh vacuum conditions, of which the most important are discussed in this progress report. Contemporary views of the chemisorption bond and the factors affecting it are discussed against the background of the adsorption of hydrogen and of carbon monoxide on single crystal surfaces of face-centered cubic transition metals. Catalytic oxidation of CO over palladium and the interaction of oxygen with nickel serve as examples of chemical surface reactions.

1. Introduction

An atom located in the surface layer of a solid occupies an intermediate position between a free atom and an atom in the bulk of a crystal in that a proportion of the chemical valency (otherwise utilized in cohesion) is unsaturated. Suitable particles impinging on the surface from the vapor phase can engage not only in the usual van der Waals interaction (= physical adsorption) but also in chemical bonding. This phenomenon, known as chemisorption, appears to be the primary step of all chemical surface processes.

Reactions on the surface of metals have eminent practical significance; it will suffice to recall the processes of heterogeneous catalysis or corrosion. In spite of tremendous scientific effort in these areas the fundamental elementary steps remain largely unknown and in the absence of reliable predictions work remains mainly empirical. The principal difficulty encountered when dealing with "real" surfaces lies in the multitude of generally uncontrollable parameters (crystallographic orientation, structural defects, impurities, substrate effects, *etc.*) affecting their chemical behavior, which are accessible only poorly, if at all, to the experimental techniques presently available.

The situation is greatly simplified if single-crystal surfaces are used having a uniform orientation which contains a minimum of foreign atoms. The latter requirement can be satisfied only under ultrahigh vacuum (UHV) conditions[1], *i.e.* at residual gas pressures of about 10^{-10} torr. In the past few years several experimental procedures have been developed for the study of such model systems, which provide highly detailed information in some cases. A parallel development has been the very recent intensification of efforts to arrive at a theoretical understanding of surface phenomena.

2. Experimental Methods

A complete description of surface processes includes the following information: The qualitative and quantitative chemical composition of the interface (including the molecular nature of adsorbed species), the geometrical structure, the energy of binding between the surface and the adsorbed particles, dipole moments of adsorption complexes, the energy distribution of electronic states, vibrations, surface diffusion, and the kinetics of ad- and de-sorption and of surface reactions. The relevant questions can be answered to various degrees of satisfaction with the aid of various modern experimental methods. Complete theoretical analysis of the experimental data still runs into considerable difficulties, however, and in some cases we are still far removed from full exploitation of the information available in principle from an experiment. Comprehensive descriptions of surface processes are clearly

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[**] Based on a Plenary Lecture delivered at the General Meeting of the Gesellschaft Deutscher Chemiker at Cologne, September 8—12, 1975.

not to be expected from the use of a single method; this will require combination of various approaches. A selection of the most powerful experimental tools currently available will be presented below.

Thermal Desorption Spectroscopy[2]

A basically simple experiment is to expose a clean surface for a given time to a given partial pressure of the gas of interest[*] at a temperature at which no significant desorption takes place, and then to continuously raise the temperature of the sample under UHV conditions while recording the partial pressure with a suitable measuring device (preferably with a quadrupole mass spectrometer). Figure 1 illustrates a series of such thermal desorption spectra from a Ni(111) surface previously exposed to different doses of hydrogen[3]. Measurements of this kind afford information about adsorption kinetics, the existence of different adsorption states, adsorption energy, the order of reaction of desorption, and (on use of isotope mixtures) the question whether adsorption is accompanied by dissociation of the molecule.

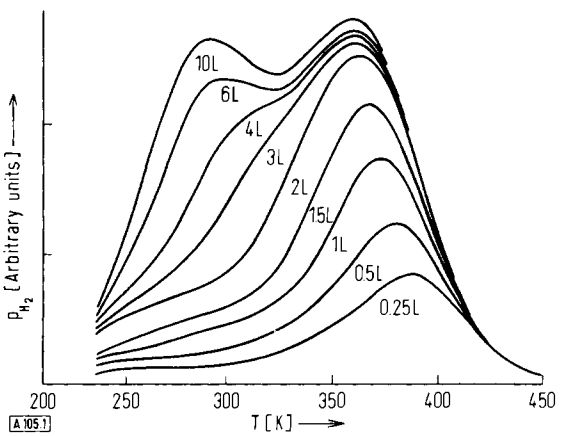


Fig. 1. Thermal desorption spectra for the H_2/Ni(111) system after covering to various extents [3] (1 L = 10^{-6} torr × s).

Change in Work Function[4]

The work function of a metal, *i.e.* the minimum energy required to remove an electron from the Fermi level to the vacuum, is modified by the presence of dipole layers on the surface—such as almost invariably arise on formation of adsorbed phases. Various techniques can be used for highly sensitive measurement of this quantity (with an accuracy of about 1 mV). This reveals the dipole moment of the adsorption complex and its possible variation with the degree of coverage. Moreover, such measurements can, after suitable calibration, provide a convenient measure for the surface concentration of adsorbed particles. If there is a reversible equilibrium between the adsorbed layer and the vapor phase, this procedure can be used for plotting adsorption isotherms from which in turn the so-called isosteric adsorption energies can be derived with the aid of simple thermodynamic relationships[5]. All the adsorption energies reported in the following sections were determined in this way.

[*] The commonest unit employed is 1 L (Langmuir) = 10^{-6} torr · s. This dose will just suffice to completely cover a clean surface with an adsorption layer if each impinging particle is adsorbed.

Secondary Ion Mass Spectrometry (SIMS)[6]

This relatively common technique involves bombardment of the solid with primary ions (usually noble gases) and mass analysis of the secondary ions or neutral particles generated. By reducing the current density of the primary beam this method can be rendered largely non-destructive while still displaying an extremely high sensitivity. The fundamental individual processes are rather complex, however, thus impeding quantitative conclusions.

Ion Backscattering Spectroscopy[7]

In this method a monoenergetic ion beam ($E < 10$ keV) is scattered at a surface and the energy of the scattered ions is analyzed. Application of the laws of conservation of energy and momentum shows that the energy spectrum of the backscattered ions is equivalent to a mass analysis of the surface atoms. This mass analysis is restricted to the outermost atoms provided that the ion energy is not too high. In favorable cases the technique also yields structural information about the position of adsorbed particles. Ion backscattering spectroscopy can, in principle, be easily combined with other methods (*e.g.* LEED and AES) but has not yet found wide application.

By far the most important group of methods is based on the analysis of the energy and/or direction of low energy electrons ($E \leq 1000$ eV) emitted from a solid surface on excitation with suitable primary radiation[8]. The average escape depth of electrons from metals is shown as a function of their energy in Figure 2. It may be seen that this quantity (d) amounts to no more than about two to three atomic layers between 40 and 400 eV, *i.e.* such electrons arise largely from the surface. Among the methods of investigating surfaces which exploit this effect the greatest significance attaches to Auger electron spectroscopy (for elemental analysis), diffraction of low energy electrons (for structural elucidation), and photoelectron spectroscopy (for determination of electronic binding energies and of surface orbitals). The instrumental armamentarium required can be combined in a single apparatus. It should be mentioned that the interaction of electrons with adsorption layers can also lead to chemical changes or desorption. This side effect, while undesirable *per se*, can also be subjected to systematic study as in the method of electron-impact induced desorption (ESD)[9].

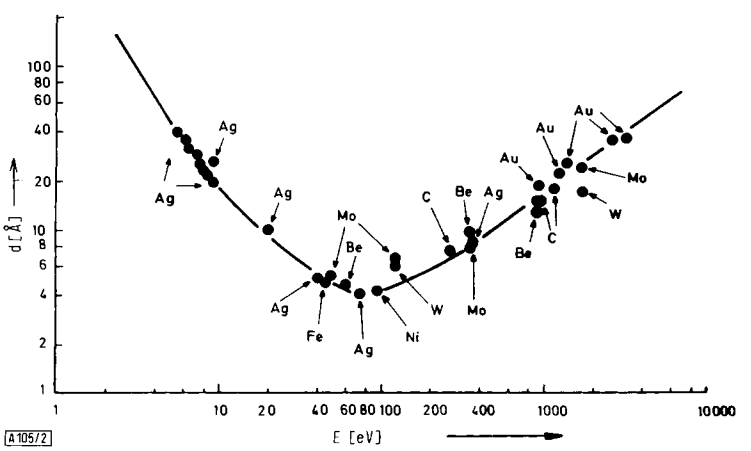


Fig. 2. Average escape depths (d) of electrons from metals as a function of their energy [8].

Auger Electron Spectroscopy[8, 10]

If an electronic core level of an atom is ionized by suitable primary radiation (preferably an electron beam) then the resulting hole is reoccupied by transition of an electron from a higher level. The liberated energy can be transferred non-radiatively in competition with X-ray fluorescence to another (bound) electron which can then be ejected from the solid with corresponding kinetic energy as a so-called Auger electron. In light elements and at energies less than 1000 eV this effect greatly predominates, thus imparting a high degree of sensitivity to the method. The experimental procedure consists in determination of the energy distribution of the emitted secondary electrons—the second derivative is usually recorded for reasons of expedience. The maxima recorded can be assigned to the elements present in the surface region. The Auger electron spectrum of a contaminated nickel surface is shown as an example in Figure 3a. The area examined is determined by the diameter of the primary electron beam and amounts to about 1 mm^2. If desired the electron beam can be focused on a much smaller spot. Line scanning of a given surface region at constant analyzer energy and simultaneous control of the brightness of an oscilloscope image by the intensities of the relevant Auger line permits measurement of the lateral distribution of individual elements on the surface ("scanning Auger"), as illustrated in Figures 3b and 3c.

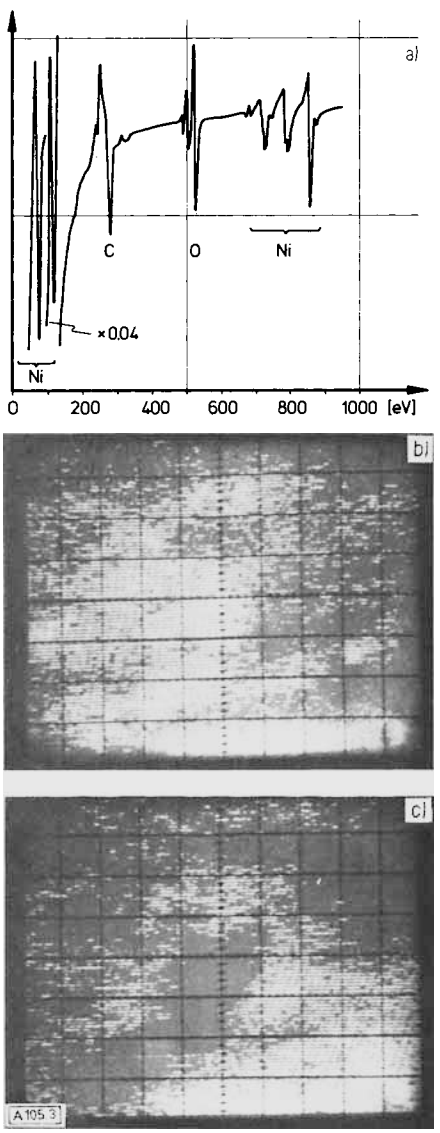


Fig. 3. a) Auger electron spectrum of a nickel surface contaminated with C and O. b) and c) Scanning Auger spectra of the lateral distribution of the elements C and O, respectively, in a surface region measuring 1 × 0.8 mm^2 (*J. Küppers*, unpublished).

Provided an element is distributed only in two dimensions on a surface, the intensity of the corresponding Auger signal is proportional to its surface concentration to a good approximation. So far, *absolute* quantitative analysis has been possible only after calibration and is therefore one of the principle unsolved problems of this method.

Low Energy Electron Diffraction (LEED)[8, 11]

A monoenergetic beam of particles having momentum mv is known to be equivalent to a material wave of wavelength $\lambda = h/mv$. For electrons of energy 150 eV, $\lambda = 1$ Å, *i.e.* interference takes place at surfaces of crystals as first demonstrated by *Davisson* and *Germer*[12]. In several respects the experimental set-up for the LEED technique resembles that for the Laue method for X-ray diffraction: a monoenergetic electron beam impinges normally on a single crystal surface and undergoes partial backscattering in those directions which satisfy the two Laue conditions for lattice periodicity parallel to the surface. Owing to the small depth of penetration of the electrons the third Laue condition (for periodicity in the direction normal to the surface) merely leads to characteristic changes in the intensity of reflections with the wave number of the electrons. After filtering out the inelastically scattered electrons, the elastically diffracted ones are post-accelerated and produce a "diffraction pattern" on a fluorescent screen. Adsorption of gases usually causes the appearance of new diffraction spots. This means that the adsorbed layer forms an ordered structure whose periodicity deviates from that of the substrate. The position of the diffraction spots reveals the unit cell of the surface structure, and in favorable cases also the mutual configuration of the adsorbed particles. Complete structural analysis—and especially determination of distances between the adsorbate and the surface atoms—from the LEED intensities is rendered very difficult by the extensive occurence of multiple scattering effects. Although an adequate theoretical approach has meanwhile been developed, this formidable task has so far only been accomplished in few cases in which adsorbed atoms form simple superstructures (O, S, Se, Te on Ni[13], I/Ag(111)[14]). So far in all instances, the positions with the maximum coordination number (4 on the (100) surface, 3 on the (111) surface) are the adsorption sites occupied.

Photoelectron Spectroscopy[15]

Irradiation of a sample with monochromatic light of sufficient energy can lead to ionization of the occupied electronic levels (with different probabilities). The emitted photoelectrons have a kinetic energy E_{kin} (disregarding multiple-particle effects), which is given by $E_{kin} = h\nu - E'_B$ (conservation of energy). E'_B is termed the "binding energy" of the liberated electron relative to the vacuum level. In general, the energy scale is referred to the Fermi level of the solid, which differs

from the vacuum level by the work function Φ. Applying *Koopmans'* theorem the experimentally determined binding energies are frequently equated to the orbital energies. However, considerable errors may then occur due to neglect of relaxation and correlation effects. Additional effects of this kind will arise compared with the free molecule owing to the presence of a solid surface: their theoretical and experimental treatment remains a largely unsolved problem, and yet a necessary requirement for any quantitative interpretation of changes in orbital energies due to chemisorption bonding.

Photoemission spectra are excited either by soft X-rays (XPS) or by UV light (UPS). The former approach affords mainly information concerning the core levels. Chemisorption levels occurring within the valence band region are better examined by UPS. Excitation is then usually accomplished with He(I) ($h\nu = 21.2$ eV) or He(II) ($h\nu = 40.8$ eV) resonance radiation. Continuous radiation of even higher photon energy is available from an electron synchrotron; however, this light source is accessible to only few researchers[16].

While UPS studies have hitherto been mainly concerned with measurements of the energy distribution of photoelectrons over a relatively large emission angle, interesting variations in intensity with the direction of emission have recently been discovered[17]. The theoretical analysis of these effects is presently undergoing rapid development[18], and holds promise of some insight into the spatial orientation of the relevant orbitals on the solid surface.

3. Mechanism of Chemisorption

Analysis of the thermal desorption spectra for the H_2/Ni(111) system illustrated in Figure 1 reveals, *inter alia*, that desorption corresponds to a second order reaction. Experiments with a mixture of H_2 and D_2 indicated complete equilibration of the isotopes on the surface. Both observations justify the conclusion that hydrogen is adsorbed in atomic form. The energy of the Ni—H bond is only 63 kcal/mol while the dissociation energy of H_2 is 104 kcal/mol. This is certainly a principal reason for the activity of nickel as a hydrogenation catalyst. The dissociative adsorption of the H_2 molecule requires no measurable activation energy, although cleavage of the free molecule needs 104.2 kcal/mol. The way in which this energy threshold is overcome by the surface can be depicted schematically as in the potential energy diagram[19] of Figure 4: on approaching the metal surface a H_2 molecule passes through a shallow energy minimum, corresponding to physisorption. In contrast, a H atom is capable of chemisorption bonding characterized by a deeper minimum closer to the surface. Intersection of the two potential energy curves below the zero point leads to dissociative adsorption without activation energy. Adsorption of hydrogen on copper involved measurable activation energy[20]; the energy curves therefore intersect above the zero energy level.

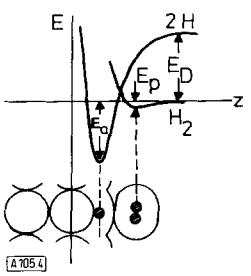


Fig. 4. Potential energy diagram according to *Lennard-Jones* [19] for adsorption of hydrogen on metals. E_D, dissociation energy of H_2 (104 kcal/mol); E_p, adsorption energy for physical (molecular) adsorption; E_a, adsorption energy for atomic chemisorption.

The occurrence of chemisorption between a H atom and a metal surface is illustrated by the energy-level scheme of Figure 5. The metal is represented as a continuum of electronic states occupied up to the Fermi level E_F. As long as the H atom is located at a long distance from the surface its 1s electron is in a state of sharply defined energy (ionization energy $I = 13.6$ eV) lying below the Fermi level of the metal (work function $\Phi \approx 5$—6 eV). A second electron in the 1s level gains only 0.75 eV in energy relative to the vacuum level owing to electron-electron repulsion so that the affinity level A lies above the Fermi level. Therefore only slight transfer of charge will be expected to occur from the metal to the adsorbed H atom, as is manifested in the small dipole moment of about 0.05 D[3] established experimentally, and the bond should be essentially covalent. On coupling of the H atom to the metal a new chemisorption level will arise which is broadened and shifted relative to the H1s orbital. The broadening of this level can be regarded as a consequence of *Heisenberg's* uncertainty principle, *i.e.* an electron has only a limited lifetime in the chemisorption level owing to tunneling to and from the metal. A somewhat different (but equivalent) approach ascribes the broadening to the continuous energy distribution of the set of molecular orbitals formed from the orbital of the adsorbed H atom and a suitable set of metal wave functions.

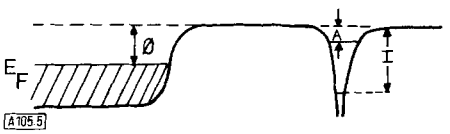


Fig. 5. Energy diagram for interaction of a H atom (right) with a metal surface (left).

The shift results from several contributory factors, *i.e.* the drop in energy due to the chemical bond, an increase due to intraatomic Coulomb interaction, and a further increase arising from the attractive interaction of the ionized atom with its image charge in the metal. A useful concept that can be introduced at this stage is that of the so-called local density of states $\rho(E)$ defined by overlap of the adatom wave function with the metal wave function at a given energy E, *i.e.* describing the energy distribution of the states generated by the chemisorption bond. To a first approximation this local density of states is directly apparent from the energy distribution measured by UV electron spectroscopy (UPS)—or more precisely in the additional emission relative to the pure metal as a result of chemisorption[21]. It should be pointed out, however, that the quantitative analysis of such spectra is still beset by serious theoretical difficulties[8, 15b].

Figure 6 shows the UPS spectra of a pure Ni(111) surface (curve a) and one covered with hydrogen (curve b)[22]. In curve a) a pronounced maximum about 2 eV wide is seen immediately below the Fermi level which arises from the emission from the Ni d band with its high density of states. (The increase on going to lower energy is attributable to the emission of secondary electrons and not to the existence

of further (lower-lying) valence states of high density of states.) After adsorption of hydrogen an additional, relatively broad maximum appears *ca.* 6 eV below E_F (*ca.* 12 eV below the vacuum level) which is identified as the above mentioned chemisorption level. The broadening may possibly also be affected by other (many-particle) effects[23].

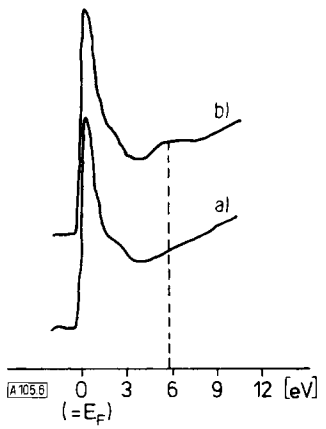


Fig. 6. UV photoelectron spectra ($h\nu = 21.2$ eV) of a) a clean Ni(111) surface and b) one covered with hydrogen.

The first quantitative theory of chemisorption of hydrogen on transition metals was developed by *Newns*[24] within the framework of the so-called Anderson formalism (see below), and considered only coupling of the H1s level with the metal d band. Fitting the adsorption energy to the experimental value affords a chemisorption level at *ca.* 6 eV below E_F, thus corresponding exactly to the additional maximum in the photoemission spectrum. A subsequent EH calculation (extended Hückel theory) for a small cluster of metal atoms showed, however, that the sp band should also play an important role in the chemisorption of hydrogen[25]. Recent confirmation has come from an extension of the formalism used by *Newns* with inclusion of the Ni sp band and of non-orthogonality effects[26]. The chemisorption level should accordingly be centered about 7 eV below E_F.

The theory of chemisorption is presently in a state of flux. It unites essential elements of the quantum chemistry of molecules with those of solid state theory[27]. An important aspect is that the metal represents an open system, *i.e.* provides an inexhaustable supply of electrons. The simplest approach is based on an LCAO-MO model utilizing a Hartree-Fock approximation. A relevant formalism was originally set up by *Anderson*[28] for the treatment of dilute alloys and later applied to the chemisorption problem[24, 26, 29]. Such calculations reveal the tendency for formation of a "surface molecule" in the case of strong chemisorption; this species is composed of the adsorbed particle and a small number of neighboring metal atoms. The latter participate directly in bonding with electronic states split off from the band of the metal utilized (as is seen to be the case in the H/Ni(111) system). The chemisorption bond thus assumes a markedly local character, suggesting a comparison with similar molecular compounds (*e.g.* in the case of CO adsorption described in Section 4 with corresponding polynuclear carbonyl complexes). Furthermore this also provides some justification for confining the theory of chemisorption to the treatment of small clusters. A particularly suitable approach is the SCF-X_α procedure developed by *Slater* and *Johnson*[30] which has already been applied with considerable success to the calculation of ionization energies in a number of systems[31].

A serious problem common to all LCAO-MO procedures is the neglect of correlation effects. These can be included in an extended Anderson model[32]. Another attempted approximation starts from the Heitler-London (VB) method (in which correlation effects are of course overemphasized)[33]. The computational effort involved in such theoretical models is much greater, however, and abandonment of the concept of one-electron states makes direct comparison with orbital-spectroscopic data difficult. The reader is referred to available surveys[27] concerning the points in favor of and against the various procedures.

4. Chemisorption of CO

Carbon monoxide is the molecule whose adsorption properties have been studied most thoroughly so far. The following discussion will be confined to a few cubic face-centered metals. The more complex CO/tungsten system was recently described by *Gomer*[34]. *Ford* has reviewed the results available up to 1970[35].

The adsorption energies of CO on nickel are 26.5 kcal/mol for the (111)-face[36] and 30 kcal/mol for the (100)-[37] and the (110)-face[38]. These values are close to the dissociation energy for $Ni(CO)_4$, *i.e.* 35 kcal/mol[39]. The analogy between carbonyl compound and adsorption complex is also apparent in other properties: adsorption of CO on nickel raises the work function of the metal by about 1.3 eV[36], which is synonymous with partial transfer of electronic charge from the metal to the adsorbate. In $Ni(CO)_4$ *ab initio* SCF-MO calculations likewise revealed an electron transfer to the ligands, producing a positive charge of about $0.5\,e_0$ at the nickel atom[40]. This electron transfer is ascribed to partial population of the $2\pi^*$ MO of the CO molecule, manifested in the IR spectrum as a shift of the CO stretching frequency to lower wave numbers[41]. Finally, comparison of the photoelectron spectra of $Ni(CO)_4$[42] and CO adsorbed on nickel[43], as shown in Figure 7 together with the spectrum of gaseous CO[44], appears remarkable. The three maxima are assigned (in order of increasing ionization energy) to the 5σ, 1π, and 4σ orbitals of CO_g. For $Ni(CO)_4$ the first maximum is due to the Ni d electrons, the following broad band corresponds to overlap of orbitals derived from the 5σ and 1π MOs of the ligand, and the third maximum arises from the CO 4σ orbital[42].

In 1964 *Blyholder* proposed[45] a donor-acceptor mechanism analogous to that responsible for bonding in carbonyl compounds to account for the adsorption of CO on metals (see Fig. 8). According to this model, an electron transfer takes place from the occupied 5σ orbital to the metal and a back-donation of metal d electrons into a chemisorption level derived from the antibonding (initially unoccupied) $2\pi^*$ MO. As a consequence, the energy of the 5σ orbital should be lowered relative to that of the 1π orbital, so that the two levels cannot be resolved in the UPS spectrum and give rise to the broad maximum observed about 8 eV below E_F. Although another interpretation was originally given for the spectroscopic data[43a], this assignment of the UPS maxima

has meanwhile been confirmed by recent theoretical[26,46] and experimental studies[43c,47].

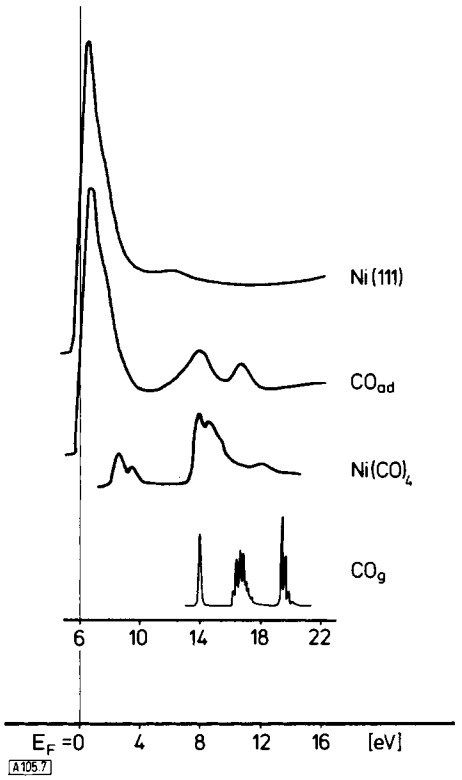


Fig. 7. UV photoelectron spectrum of CO adsorbed on Ni(111) compared with the spectra of $Ni(CO)_4$ and gaseous CO.

A theoretical study[26] has indicated that some 50% of the adsorption energy of CO on a Ni(111) surface (*i.e.* 13 kcal/mol) should arise from coupling of the 5σ orbital to the metal sp bands. In the case of the corresponding surface of the neighboring element copper, coupling of the d electrons to the $2\pi^*$ orbital should play only a very minor role, as

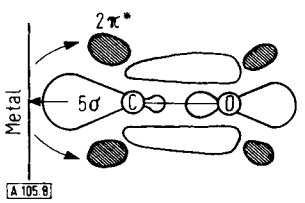


Fig. 8. Donor-acceptor mechanism for the adsorption of CO on metal surfaces.

is confirmed by the far lower adsorption energy of about 12 kcal/mol[43d] and by the reverse sign of the dipole moment (*i.e.* negative excess charge on the metal side)[48]. Table 1 lists the CO adsorption energies for the (111)-faces of various cubic face-centered transition metals. It should be noted that

Table 1. Adsorption energies [kcal/mol] for CO on the (111) faces of cubic face-centered metals [49].

	Ni	Cu
	26.5	12
	Pd	Ag
	34	6.5
Ir	Pt	
33	35	

in all cases except silver the adsorption structures are characterized by identical LEED superstructures, *i.e.* identical surface configurations. The differing adsorption energies are therefore due primarily to the "electronic" factor, *i.e.* the influence of the electronic properties of the solid.

The difference between Pd and Ag is particularly striking. In this context, interesting points arise in connection with the use of alloys. Figure 9 shows the variation of CO adsorption energy as a function of the change in work function (which is a measure for the degree of coverage) for Ag/Pd alloys having various surface compositions[50]. It is seen that for all samples E_{ad} attains the value for pure Pd at very low coverages but at higher surface concentrations even low amounts of Ag bring about a drastic reduction of the adsorption energy, *i.e.* the surfaces become energetically heterogeneous. A qualitative explanation of these findings results from the electronic properties of such alloys, according to which the components essentially retain their electronic structure[51] (thus in Cu/Ni alloys there are still unoccupied d states at the Ni sites, even at high Cu contents[52]) and do not form a "collective" d band, in contrast to former views. Of course it should always be borne in mind in all experiments on alloys that the composition of the surface can deviate considerably from that of the bulk and therefore requires specific careful examination[53].

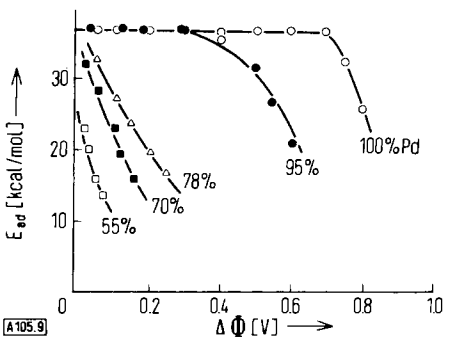


Fig. 9. Adsorption energy for CO on (111) surfaces of Ag/Pd alloys of various surface composition as a function of the change in work function $\Delta\Phi$ [50].

The "geometric" factor embraces the change in adsorption properties, on the one hand with the position of the adsorbate relative to the position of the metal atoms for a given single crystal face, and on the other with the crystallographic orientation, inclusion of structural defects representing a natural extension. These aspects will now be considered with the aid of adsorption of CO on palladium[54].

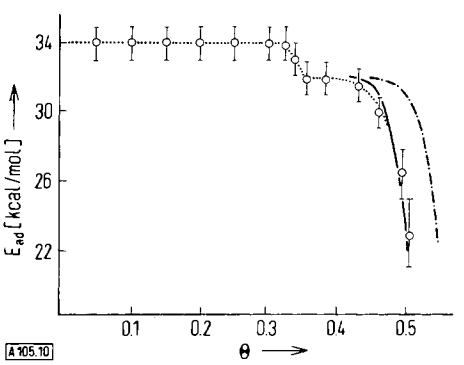


Fig. 10. CO/Pd(111). Adsorption energy as a function of a degree of coverage Φ [55].

Figure 10 shows the variation in the isosteric adsorption energy for CO on Pd(111) as a function of the degree of coverage Θ[55]. E_{ad} is seen to remain constant up to $\Theta = 1/3$, and then suddenly falls by 2 kcal/mol as the degree of coverage further increases. At $\Theta = 1/3$ the LEED diffraction pattern contains additional spots of a superstructure whose pertinent structural model is reproduced in Fig. 11 a. Up to that coverage, all CO molecules can apparently occupy identical energetically

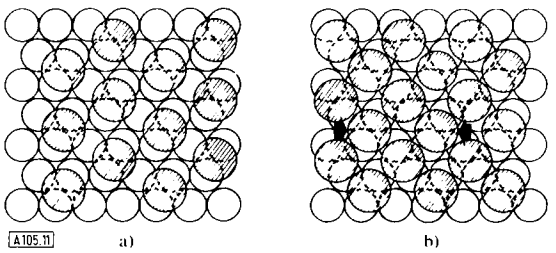
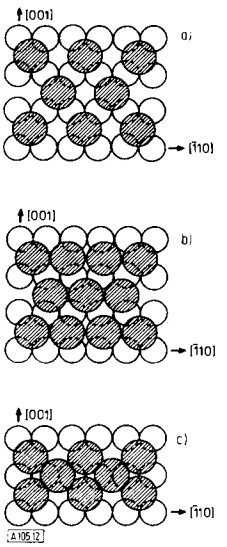


Fig. 11. Structural model for the configuration of adsorbed CO molecules on a Pd(111) surface. a) $\Theta = 1/3$; b) $\Theta = 1/2$: this structure arises by continuous compression of the unit cell shown in a) [55].



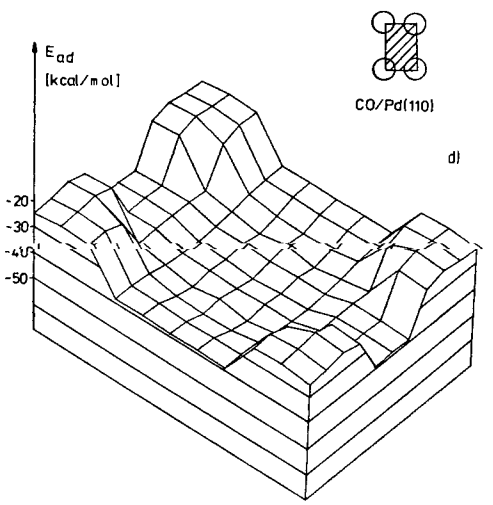


Fig. 12. a)—c) Structural models for the configuration of adsorbed CO molecules on a Pd(110) surface [54]: a) $\Theta = 1/2$; b) $\Theta \approx 3/4$; c) $\Theta = 1$.—d) Theoretical energy profile for the variation of the CO adsorption energy within the unit cell of the Pd(110) surface [26].

favorable sites without engaging in mutual interactions. (Whether these adsorption sites correspond to the "bridging positions" drawn or should be assigned to points between three Pd atoms cannot yet be decided but is immaterial for the present discussions.) As soon as the degree of coverage exceeds the value 1/3 the unit cell of the adsorbate structure is continuously compressed (cf. Fig. 11 b). Surface saturation is characterized by a kind of densest packing of the adsorbed molecules, their "size" corresponding to a diameter of about 3 Å in the present case; this value agrees fairly well with the van der Waals diameter of the CO molecule in the gaseous state[56]. The dot-dash curve in Figure 10 representing the decrease in E_{ad} with increasing Θ was calculated from these data and shows fairly good agreement with experimental data.

Similar behavior was noted for adsorption of CO on a series of other surfaces[36, 38, 49b, 49c, 54, 57]. As a further example, Figure 12 depicts the structural models for the three ordered structures of CO on Pd(110) which are successively formed with increasing degree of coverage[54]. In addition, this figure also shows a theoretically derived energy profile for the variation of the adsorption energy with the position of the CO molecule with respect to the Pd atoms[26]. (This energy profile deviates slightly from a previously published version[29b] owing to the subsequent introduction of coupling between the 5σ orbital and the metallic s electrons.) The position of most favorable energy is accordingly seen to lie between four Pd atoms. However, the area required by the CO molecules precludes occupation of each one of these positions, and an initial closing up of the adsorbed particles along the grooves in the [1̄10]-direction will take place up to about $\Theta = 0.75$. On further increase of the degree of coverage, the less favorable bridging positions will also be occupied until saturation is reached (Fig. 12c).

The general conclusion drawn from these observations is that the CO molecules do not seem to be fixed at specific adsorption sites. Instead, relatively slight differences exist in the adsorption energy over a surface, which permit a relatively high mobility of adsorbed molecules on the one hand, but also lead to a tendency to seek out a compromise between a densest packing and the periodicity of the substrate lattice, which determines the energy minima, for the arrangement of molecules on approaching the saturation limit. An analogy is observed with the polynuclear carbonyl compounds where the maximum number of ligands is likewise determined by their spatial requirements. Moreover, dynamic ^{13}C-NMR studies showed that geometric fixation of the CO molecules already gives way to fast site exchange phenomena at relatively low temperatures[58]. There is no longer any tendency to close packing for small adsorbed particles such as H, O, or N, where the great demand on surface valences for chemisorption bonding limits maximum coverage.

The variation in the initial adsorption energy (*i.e.* the value obtained by extrapolation to $\Theta = 0$) for CO on a series of variously oriented Pd single crystal surfaces is shown in Table 2. Remarkably, this quantity varies by only about 15% although the number of nearest neighbors of the metal atoms varies between 9 [(111)-face] and 6 [(311)-face]. Similar observations have also been recorded *e.g.* for the CO/Ni[36], H_2/Ni[3], and H_2/Pd systems[59], but the experimental data still appear too sparse to justify any general conclusions. Nevertheless, an interesting parallel can be drawn with the finding that numerous reactions occurring on "real" catalysts are not

affected by particle size, *i.e.* are largely insensitive to the structure of the catalyst surface[60].

Table 2. Adsorption energies [kcal/mol] for CO on variously oriented single crystal faces of Pd.

Face	(111)	(100)	(110)	(210)	(311)
E_{ad}	34	36.5	40	35	35.5

One possible way of conferring a closer resemblance to "real" surfaces upon the single crystal surfaces employed as models consists in introducing periodic arrangements of atomic steps which can be conveniently analyzed by the LEED method[61]. No measurable changes in bond energy were recorded for the adsorption of CO on a stepped Pd(111)-surface[54], while a (relatively slight) effect was established on adsorption of hydrogen[59]. Drastic differences between "flat" and stepped Pt(111)-surfaces were found by *Somorjai et al.*[62] for the kinetics of reactions with hydrocarbons.

Hitherto, only the adsorption of the undissociated CO molecule has been discussed. In spite of its high dissociation energy this molecule decomposes fairly easily above 200 °C on nickel surfaces, and even at room temperature on iron surfaces. Studies on the CO/Ni(110) system[63] showed that the carbon atoms eventually unite to form thin layers of graphite which can be reoxidized to CO by oxygen; on the other hand the adsorbed oxygen atoms can react with CO to give CO_2. This rationalizes the mode of action of these metals as catalysts for establishing the Boudouard equilibrium.

5. Interactions between Adsorbed Particles and Surface Reactions

The surface configurations of adsorbed CO molecules mentioned in the previous section can be largely understood in terms of direct through-space interactions owing to the incipient mutual interpenetration of electron shells and dipole-dipole repulsion. However, other long-range interactions frequently also occur (especially with strongly bound small atoms like H, O, or N) which are of an indirect nature (through bond) and are attributable to a coupling *via* the metal electrons involved in the chemisorption bond. Theoretical treatments of this problem[64] have shown that such interactions have an oscillatory character, *i.e.* they may be attractive or repulsive. The adsorbed particles then preferably occupy highly symmetric adsorption sites determined by the periodicity of the substrate lattice. Use of a lattice-gas model of this kind and assuming certain interaction energies permits simulation of thermal desorption spectra[65], the formation of defined LEED superstructures[66], and the appearance of order-disorder transitions[67]. The last-named phenomena represent the two-dimensional analog af phase transitions, such as are known for ordered alloys or ferromagnetic substances, and can be monitored by means of the change in the LEED intensities with temperature[68]. Available data would indicate such interaction energies between adjacent adsorbed particles are several kcal/mol at maximum.

If two different kinds of species A and B are present on the surface then, by analogy with the "normal" thermodynamics of mixed phases, two limiting cases can be discerned, which are likewise basically due to intermolecular interactions[69]:

1) A and B form an ordered mixed phase *(cooperative adsorption)*, the surface configuration and binding energies possibly being different from those of the pure single component adsorption phases. Such an example is provided by the system of H+CO on Ni(111)[70].

2) A and B are completely immiscible *(competitive adsorption)*, *i.e.* the surface exhibits separate domains of the two adsorbed species.

The second case has been observed, *e.g.* in the interaction of oxygen and carbon monoxide with a Pd(111) surface[55] and rationalizes the kinetics of steady-state CO_2 formation. The individual steps of this reaction[71] are listed in Table 3.

Table 3. Steps involved in catalytic oxidation of CO on palladium.

CO	+ *	$\rightleftharpoons$	CO_{ad}	
O_2	+ *	$\rightleftharpoons$	$2\,O_{ad}$	
O_{ad}	+ CO_{ad}	$\rightarrow$	CO_2	*Langmuir-Hinshelwood*
O_{ad}	+ CO	$\rightarrow$	CO_2	*Eley-Rideal*
CO_{ad}	+ $1/2\,O_2$	$\nrightarrow$	CO_2	

The O_2 is adsorbed dissociatively with an adsorption energy of about 60 kcal/mol (CO, 34 kcal/mol) on regions not yet occupied by CO_{ad}. CO molecules impinging from the gas phase onto a surface occupied by O_{ad} react very rapidly, even below room temperature, to give CO_2 which immediately desorbs (Eley-Rideal reaction). Conversely, a surface covered with CO_{ad} ($\Theta_{CO} > 2/3$ max. CO coverage) completely inhibits adsorption or reaction with O_2 although a gain in energy would be associated with displacement of CO_{ad}. If both kinds of particle are located on the surface, then they occupy separate domains having diameters of at least 50–100 Å. The reaction between O_{ad} and CO_{ad} (Langmuir-Hinshelwood reaction) proceeds somewhat slower than that between O_{ad} and CO, and requires an activation energy of 7 kcal/mol[72]. As a consequence of these steps, a steady state formation of CO_2 is only expected if sufficient surface sites are made available for adsorption of O_2 as a result of thermal desorption of CO. The reactant CO thus inhibits the reaction and its desorption becomes rate determining. Figure 13 illustrates this situation with the aid of measurements of the steady state rate of formation of CO_2 and the surface concentration of CO_{ad} as a function of temperature[72].

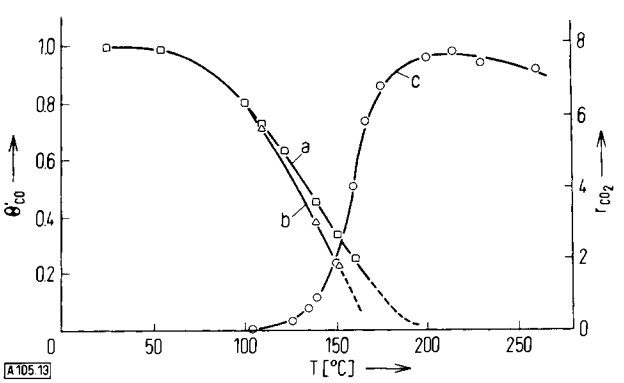


Fig. 13. Catalytic oxidation of CO on a Pd(111) surface: Steady state formation rate r_{CO_2} of CO_2 and relative degree of CO coverage $\Theta'_{CO} = \Theta_{CO}/\Theta_{CO,max}$ as a function of temperature. Curve a, Θ'_{CO} for $p_{CO} = 8 \times 10^{-9}$ torr in absence of O_2; curve b, Θ'_{CO} in a reaction mixture with $p_{O_2} = p_{CO} = 8 \times 10^{-9}$ torr; curve c, r_{CO_2} (in relative units) at $p_{O_2} = p_{CO} = 8 \times 10^{-9}$ torr [72].

A similar situation applies to the catalytic oxidation of CO on single crystal surfaces of Pt[73], Ru[74], and Ir[49b]; modifications are attributable to differing strength of the M—O bond, which renders the reaction O_{ad} + CO rate determining in the case of nickel[75].

Interaction between oxygen and nickel represents another kind of surface reaction leading to formation of three-dimensional compounds (oxide). During the action of O_2 on pure Ni(111) or Ni(100) surfaces formation of chemisorption structures is first observed whose unit cells are related in a simple manner to the periodicity of the metal lattice[76, 77]. In the case of the $c2 \times 2$ structure on Ni(100) the LEED intensities were subjected to detailed theoretical analyses[13]. Each O atom was accordingly found to be located between four Ni atoms at a perpendicular distance of 0.9 Å. The increase in the work function reveals a slight excess negative charge at the oxygen atom. The UPS spectrum[78] (curve b in Fig. 14) exhibits an additional maximum about 5.5 eV below the Fermi level, shown by cluster calculations[79] to arise from chemisorption levels derived from O 2p states. The energy distribution of the Ni d electrons remains largely unaffected at this stage.

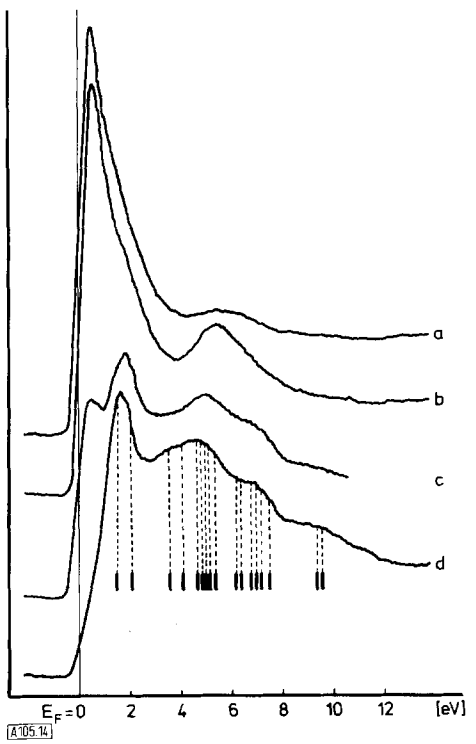


Fig. 14. UV photoelectron spectra ($h\nu = 40.8$ eV) pertaining to the interaction between O_2 and a Ni(111) surface [78]. a, clean surface; b, with a chemisorbed oxygen layer; c, transition to oxide; d, after formation of an epitaxial NiO layer.

After saturation of the chemisorption layer further uptake of oxygen is much slower and leads to formation of an epitaxial NiO layer just a few atomic layers thick[77, 78]. The UPS spectrum (curve c) now also displays drastic changes in the region of the Ni d band. Continuous growth of a thick NiO layer then represents the third stage of this reaction. In the UPS spectrum (curve d) the emission from the metallic d band has completely disappeared, being replaced by a maximum at about 1.7 eV which is assigned to the d states of the Ni^{2+} ions in NiO. Furthermore, a fundamental change observed in the remaining spectrum is in good agreement with the excitation energies calculated for a NiO_6^{10-} cluster[80]. Transition to the oxide is also observed in a discontinuous change in the binding energy of the Ni 2p electrons[81]. As an overall conclusion, it follows that the oxygen chemisorption complex and the oxide are two clearly distinguishable phases whose transformation is not associated with a continuous variation of the valence state or structure.

6. Conclusion

The examples presented in this survey are merely a fraction of the information available and are intended mainly to illustrate the insights into chemical processes occurring on metal surfaces provided by present-day techniques. Apart from further development of experimental and theoretical methods, the main task of the future will be to throw a bridge from the model systems to the situations encountered in practice.

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Mechanistic Aspects of Olefin Metathesis

By N. Calderon, E. A. Ofstead, and W. A. Judy[*]

In this paper views regarding the nature of the transition state in olefin metathesis are discussed. Earlier concepts that assumed a pairwise scrambling mechanism have been recently challenged. Metathesis studies involving acyclic as well as cyclic olefins have been reported which strongly suggest a chain process that may involve a carbene-to-metallocycle interconversion as the pathway responsible for transalkylidenation. Catalytic systems that display a low apparent metathesis activity on terminal olefins display a unique specificity in cross reactions with internal olefins. Critical experiments indicate that terminal olefins rapidly undergo regenerative metathesis preferentially. Results suggest that in the transient metallocycle, the most stringent steric requirements occur at the β-carbon, although the origin of this steric demand is not obvious.

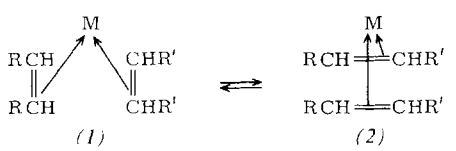
1. Introduction

The results of key experiments which extablished the site of bond cleavage in olefin metathesis[1-3] generated an extensive quest for a mechanism that could rationalize the various aspects of a remarkable new catalytic reaction. Ideally, if one is to obtain a coherent description of a catalytic process on an atomic scale, it is necessary to establish: a) the structure of the catalytic site, b) logistic aspects, *i. e.*, pathways by which incoming reactants replace outgoing products, and c) the nature of the transition state and the intimate electronic transformations that occur along the reaction coordinate.

Characterization of catalyst sites in processes that are promoted by transition metals is not easily accomplished. Many diverse catalysts promote olefin metathesis. These encompass uni- and multicomponent systems derived from various metals having different oxidation states, and may be homogeneous or heterogeneous in nature. Hence, the assignment of a particular structure as being the "true" description of the catalytic site is virtually impossible.

The relevance of ligand exchange processes to the logistics aspect of olefin metathesis is clear. An outstanding feature of certain metathesis catalysts is their capacity to promote rapid reactions at very low concentrations. Extremely fast rates are common, and these could not be realized if an efficient route did not exist for the exchange of incoming and outgoing olefin molecules on the active site of the metal. Using rhodium complexes, *Cramer*[4] demonstrated that ligand exchange processes may proceed by either S_N2 or S_N1 mechanisms, depending primarily on the ligand field surrounding the metal and the availability of coordination sites.

Views regarding the nature of the transition state in olefin metathesis are in a state of flux. Until recently, most proposed schemes for the transalkylidenation process assumed a pairwise scrambling that required an initial bisolefin-metal entity *(1)* bearing two olefinic ligands in a *cis* configuration about the metal. Subsequently, a controversy developed over the detailed nature of the transformation of this complex *(1)* into the corresponding product complex *(2)* [Eq. (a)][*].



(1) *(2)* (a)

Thus, concepts such as quasicyclobutane[5], tetramethylene-metal complex[6], and metallocyclopentane[7] were proposed in attempts to describe the intervening transition state. The fact that a bisolefin-metal complex of type *(1)* has never been isolated for any active metathesis catalyst, lent all of the aforementioned schemes a certain degree of vulnerability. Lately, several publications disclosed results that appear to be incompatible with the reaction pathway depicted in Eq. (a). Rather, they point to a non-pairwise chain mechanism that favors a single olefin molecule complexed to a carbene-bearing metal undergoing interchange *via* a metallocyclobutane intermediate [Eq. (b)][**].

$$\begin{matrix} R'CH{=}M \\ R'CH{=}CHR \end{matrix} \rightleftharpoons \begin{matrix} R'CH \\ \| \\ R'CH \end{matrix} \quad \begin{matrix} M \\ \| \\ CHR \end{matrix} \qquad \text{(b)}$$

The intent of this article is to present an up-to-date account of recent developments toward understanding the mechanism of olefin metathesis, and to compare the relative merits of the two basic schemes. In addition, a discussion is included on a recently discovered characteristic of catalysts which display a low apparent activity with terminal olefins. These have been found to react with mixtures of terminal and internal olefins resulting in the selective formation of cross metathesis products.

2. Vulnerabilities in Pairwise Scrambling Schemes

2.1. Polymerization of Cycloolefins

Dolgoplosk[8] suggested that the formation of a high molecular weight product during the initial stage of a cycloolefin metathesis polymerization was inconsistent with a pairwise scrambling mechanism. Indeed, high molecular weight polymers are commonly observed during early stages of cy-

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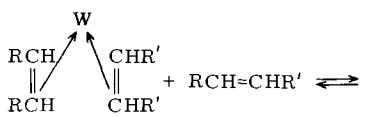
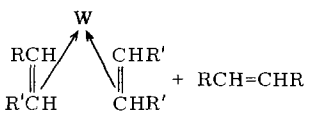
[*] Here and in the following equations the ligands to metal atom M external to the olefin have in most cases been omitted.

[**] For sake of clarity, here and in the following equations the carbene-metal bond has usually been drawn as a double bond; for the character of this bond see Section 4.

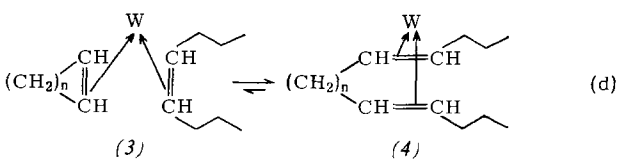
cloolefin polymerizations. For example, the polymer obtained at 6% conversion from cyclooctene using a $WCl_6/C_2H_5OH/C_2H_5AlCl$ catalyst had a molecular weight of about 200000–300000[9]. (This product was accompanied by low molecular weight macrocyclic oligomers not included in the molecular weight value.) This phenomenon requires that cycloolefin polymerizations propagate by some type of chain process rather than by a stepwise growth process. Such a process is nevertheless reconcilable with a pairwise scheme when certain restrictions are invoked[10]. The pairwise mechanism [Eq. (a)] could exhibit a chain reaction character if the rate of the transalkylidenation step were much faster than that of the exchange



(c)



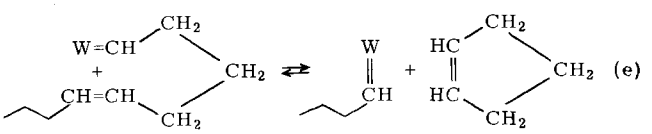
step [Eq. (c)], and if in the propagation step the equilibrium between *(3)* and *(4)* were to lie far on the side of the bidentate complex [Eq. (d)].



(3) *(4)* (d)

On the other hand, if reaction (c) were faster than reaction (a), a transfer-to-monomer process would predominate in the early stages of cycloolefin metathesis, resulting initially in a preponderance of low molecular weight cyclic oligomers and essentially no high molecular weight product.

Chauvin et al., who were first to suggest non-pairwise transalkylidenation *via* a carbene-metal intermediate [see Eq. (b)][11], recently examined the effect of conversion on molecular weight distributions of polymers and copolymers obtained from cyclopentene and cyclooctene[12]. The monomer-polymer and polymer-oligomer equilibria were presented as "back-biting" processes. Hence, for cyclopentene the propagation-depropagation equilibrium involved an intramolecular carbene-metal interchange as depicted in [Eq. (e)].



(e)

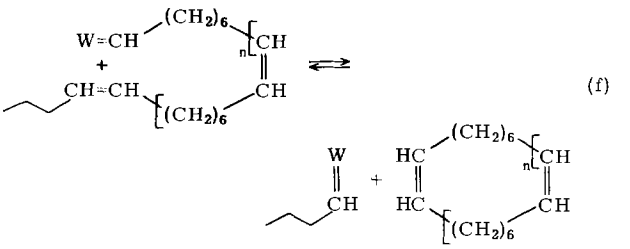
In a similar fashion, the formation of macrocyclic oligomers in cyclooctene polymerization is illustration in Eq. (f).

Two significant points evolve from the non-pairwise scheme illustrated here:

a) The high molecular weight polyalkenamers are linear, even when acyclic olefins are absent in the reaction.

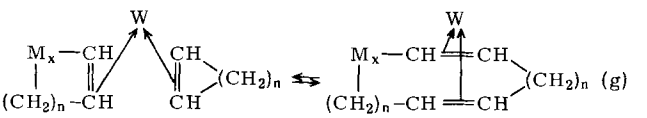
b) Cyclic oligomers are not formed *via* intermolecular condensation of two smaller rings.

In contrast to the above scheme, cycloolefin metathesis *via* a pairwise interchange process predicts that, in the complete



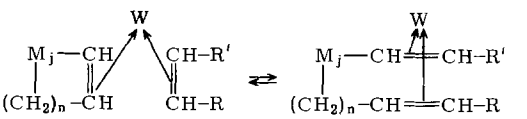
(f)

absence of acyclic olefins, propagation proceeds by macrocyclization as in Eq. (g)[13].



(g)

Linear, open chain macromolecules would be obtained by cross metathesis with acyclic olefins as depicted in Eq. (h) where the acyclic alkylidene moieties become chain ends:



(h)

Furthermore, this mechanism affords cyclic oligomers by both inter- and intramolecular metathesis.

Studies to determine whether polyalkenamers are linear or macrocyclic have been reported by *Scott*[14,15]. By adding varied amounts of chain scission agents to a cycloolefin metathesis and examining their effect on product molecular weight, it was possible to establish the acyclic nature of the high molecular weight polyoctenamer. Figure 1 is a plot of $1/D'$, the reciprocal of the number-average degree of polymerization (determined by vapor phase osmometry), versus τ, the ratio of reacted 3-hexene to cyclooctene. The three lines are theoretical behavior curves for three different cases. Curve A is for the random scission of a mixture of polymer chains which is entirely acyclic, curve B is the theoretical expression for the scission of a mixture of rings and chains, and curve C the case of random scission of cyclic macromolecules. The mathematical derivation of the respective expressions that

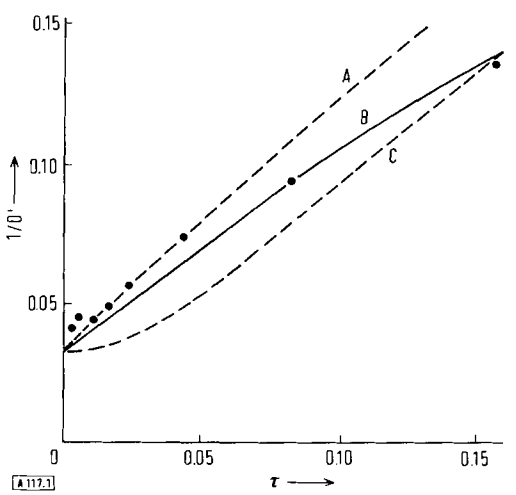


Fig. 1. Dependence of the reciprocal of the number-average degree of polymerization, D', on the mole ratio of reacted 3-hexene to cyclooctene, τ. Theoretical curves are A: all linear chains; B: ring-chain equilibrium; and C: all cyclic polymers.

produce these curves is fully described in ref. [14]. The agreement between the experimental points and curve B is striking. It lends considerable support to the assertion that, in the *absence of any deliberately added acyclic olefin*, polyoctenamer as prepared under the conditions used in that study consisted of high molecular weight linear chains (80—85 % by wt.), while the remaining low molecular weight species were cyclic oligomers having an average molecular weight of about 500.

Extending this work to polypentenamer, *Scott*[15] examined the effect of conversion on the weight-average and number-average molecular weights, as well as the molecular weight distribution. This study revealed that polypentenamer was linear in structure as was polyoctenamer.

The experimental verification that high molecular weight polyalkenamers are linear and not macrocyclic has a limited significance for the mechanism of olefin metathesis. It is compatible with the non-pairwise interchange concept, such as the carbene-metal scheme proposed by *Herisson* and *Chauvin*[11], but it does not exclude entirely the pairwise transalkylidenation scheme. It is recognized that the final, necessary and sufficient condition for ring-chain equilibria, as observed[14-16] and described above[12], is the presence of a trace amount of chain scission reactant, typically an acyclic olefin. Thus, the pairwise scrambling mechanism can be reconciled with the formation of linear chains even when end-groups are not introduced deliberately into the system, if one takes into account (a) the possible *in situ* formation of chain ends during the reaction of the organoaluminum catalyst component with the tungsten salt; or (b) the presence of very small amounts of olefinic impurities.

2.2. Formation of Cyclic Oligomers

Three basic features were established in a study[13] related to the formation of oligomers during cycloolefin metathesis:

1. The oligomers are macrocyclic.
2. The population of macrocyclics is controlled primarily by the double bond frequency along the polymeric chain.
3. The oligomeric macrocyclics and their corresponding high molecular weight polyalkenamer are interconvertible.

As stated earlier, whereas pairwise interchange schemes allow formation of macrocyclic oligomers by two routes, intramolecular "pinching-off" of a cyclic entity from a higher macromolecule and intermolecular condensation of two smaller rings, the carbene-metal scheme provides only one route for cyclic oligomer formation, namely, intramolecular "back-biting" [Eq. (e) and (f)]. By determining quantitatively the relative abundance of the various macrocyclics produced during the metathesis of 1,5-cyclooctadiene, it was demonstrated that these are produced exclusively by an intramolecular process[17, 18].

1,5-Cyclooctadiene is known to yield two series of macrocyclics. One contains "whole" multiples of the monomer $[(C_8H_{12})_n]$, the others may be described as "sesqui-oligomers" $[(C_8H_{12})_n—C_4H_6$, where $n \geq 2]$. Table 1 presents the relative concentrations of the respective macrocycles—the "whole" oligomers (C_{16}, C_{24}, C_{32}...) and the "sesqui-oligomers" (C_{12}, C_{20}, C_{28}...). The results indicate that the molar ratios of the various "sesqui-oligomers" relative to C_{16}, as well as the molar ratios of the "whole" oligomers to C_{16}, remain essentially constant throughout a conversion range of 1.3-to-98.5 %. (The only variant is the C_{12}/C_{16} ratio at 98.5 % conversion, which has been rationalized[18].)

To appreciate the significance of these results one must recognize that, irrespective of the mechanism invoked, the C_{12} oligomer(1,5,9-cyclododecatriene) cannot be produced by any intermolecular process, since the smallest precursor available is a C_8 ring. On the other hand the C_{16} oligomer (1,5,9,13-cyclohexadecatetraene) might be produced, at least in principle, by inter- as well as intramolecular processes. The fact that a significant amount of the C_{12} product was present even at the lowest conversions measured, and that its relative abundance remained constant throughout the course of polymerization is indicative that only one pathway for the formation of cyclic oligomers is operative, namely, an intramolecular process. This argument applies also for the higher oligomers, as clearly indicated in Table 1.

Table 1. Molar ratio of cyclic oligomers $(C_8H_{12})_n$ and sesquioligomers $(C_8H_{12})_n—C_4H_6$ to cyclohexadecatetraene ($C_{16}/C_{16} = 1.0$) (after Ref. [18]).

Conversion [%]	C_{12}/C_{16}	C_{20}/C_{16}	C_{24}/C_{16}	C_{28}/C_{16}	C_{32}/C_{16}
1.3	0.47	0.65	—	—	—
3.2	0.51	0.63	0.32	0.18	—
7.9	0.55	0.63	0.27	0.24	—
9.5	0.48	0.62	0.28	0.25	0.10
19.5	0.52	0.59	0.31	0.27	0.10
36.3	0.52	0.56	0.32	0.18	0.13
51.1	0.51	0.58	0.33	0.26	0.13
61.2	0.53	0.54	0.30	0.19	0.10
98.5	0.93	0.65	0.27	0.23	0.14

Although the data presented above are quite compatible with a non-pairwise metathesis mechanism, they still do not entirely discount the pairwise reaction pathway. The data can be accommodated with a pairwise mechanism by invoking the following kinetic assumptions:

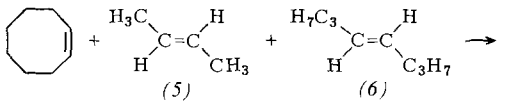
$$\begin{array}{ccccc} (C_4)_{2m} & \rightleftharpoons & (C_8)_m & \xrightarrow[k_p]{+C_8} & (C_8)_{m+1} \\ \Big\downarrow\uparrow k_e & & & & \\ (C_4)_{2m-n} & + & (C_4)_n & & n \geq 3 \end{array} \qquad \text{(i)}$$

In Eq. (i), C_8 denotes 1.5-cyclooctadiene monomer which adds to a $(C_8)_m$ polymer yielding $(C_8)_{m+1}$ with a rate constant for this step of k_p. Since $(C_8)_m$ is structurally indentical to polybutenamer, it may also be represented as $(C_4)_{2m}$. This macromolecule at all times is reversibly interconverted to the respective cyclic oligomer series $(C_4)_n$. If $k_p \gg k_e$, conditions result wherein oligomers are formed *via* the intramolecular route exclusively.

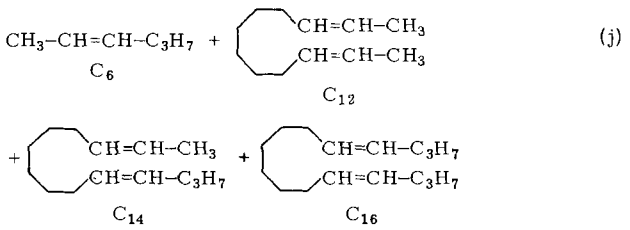
2.3. Cross Metathesis of Acyclic Olefins with Cycloolefins

Cross metathesis studies between acyclic and cyclic olefins, conducted for the purpose of examining telomer compositions, have been reported on different occasions[11, 17-22]. Perhaps the most relevant work with respect to pairwise *vs.* non-pairwise mechanisms is the one disclosed recently by *Katz*[22]. The telomer distribution produced during the early stages of the cross metathesis of cyclooctene with a mixture of *trans*-2-butene and *trans*-2-octene, in the presence of a molybdenum-based catalyst, was monitored. In addition to a

C_6, the cross product of 2-butene and 4-octene, two symmetrical (C_{12} and C_{16}) and one unsymmetrical (C_{14}) dienes were formed [Eq. (j)].



(5) *(6)*



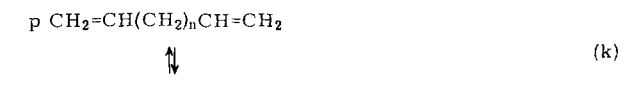
(j)

(In addition, one would expect formation of higher telomer homologs. These were not discussed.) *Katz's* contention was that, if any of the pairwise scrambling schemes were to prevail, the ratios of the unsymmetric to symmetric dienes, C_{14}/C_{12} and C_{14}/C_{16}, would be zero initially. The experiments revealed that the C_{14}/C_{12} and C_{14}/C_{16} ratios were significantly different from zero at the initial stage of the reaction; in fact, the extrapolated values at zero time suggested that the unsymmetric diene was favored initially. This kinetic study strongly supported a non-pairwise reaction scheme, such as the carbene-metal concept, but it did not entirely exclude pairwise schemes. *Katz* conceded that the discriminating merit of his experiment holds true only if one assumes that the transalkylidenation step in pairwise scrambling mechanisms [Eq. (a)] is the rate determining step. However, if the exchange step were rate determining [Eq. (c)] his data could be accounted for by either scheme.

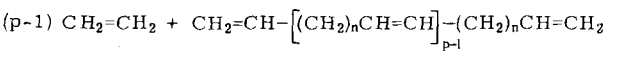
2.4. Metathesis of α,ω-Dienes

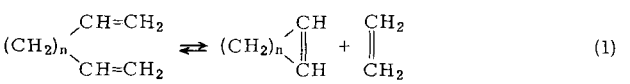
Nonconjugated α,ω-dienes, when treated with a metathesis catalyst, may undergo either metathetical polycondensation[23] forming open chain oligomers with terminal double bonds [Eq. (k)], or they may undergo intramolecular metathesis[19] to form a cycloolefin [Eq. (l)]. Both processes will yield ethylene.

The factor which determines which process will prevail at equilibrium depends primarily on the value of *n*, which correlates with the relative thermodynamic stability of a given $+(CH_2)_nCH{=}CH+$ sequence in a ring *versus* a chain. For example, *Dall'Asta*[23] metathesized 1,4-pentadiene and 1,5-hexadiene exclusively to higher molecular weight linear oligomers because the corresponding monomeric cycloolefins



(k)

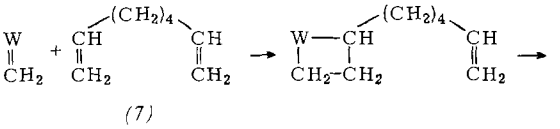




(l)

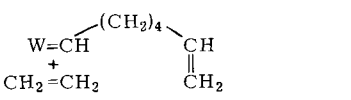
are highly strained. On the other hand, *Kroll*[24] was able to convert 1,7-octadiene to the stable product cyclohexene with 99 % selectivity.

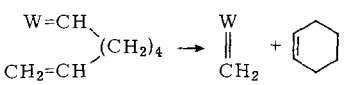
1,7-Octadiene is a substrate which is uniquely suitable for mechanistic studies. There is good evidence to indicate that: a) 1,7-octadiene does not undergo intermolecular metathesis according to Eq. (k), and b) the cyclohexene produced during intramolecular cyclization does not participate in further metathetic processes. These features were exploited by *Grubbs*[25], who studied the metathesis of a mixture of 1,7-octadiene with [1,1,8,8-D_4]-1,7-octadiene, in an attempt to distinguish between a non-pairwise chain mechanism and the pairwise scheme. The non-pairwise path is visualized as shown in Eq. (m) and (n).



(7)

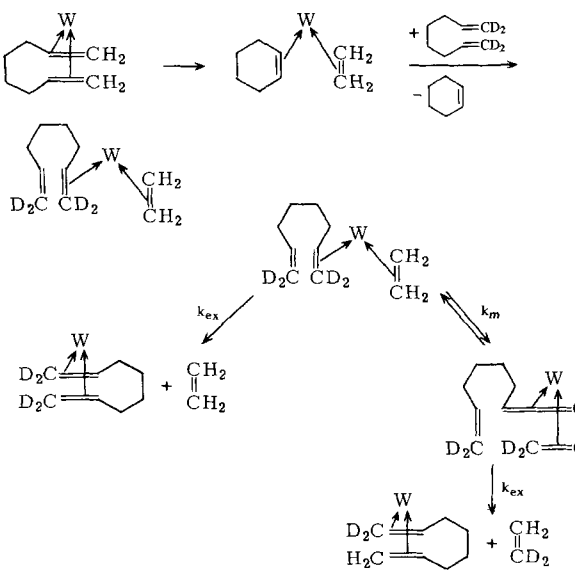
(m)





(n)

It can be demonstrated that for an equimolar mixture of *(7)* and [1,1,8,8-D_4]-*(7)* one expects to obtain a statistical distribution (1:2:1) of [D_4]-, [D_2]- and [D_0]-ethylene at low conversion even in the absence of ethylene redistribution reactions. On the other hand, the pairwise path predicts different distributions of the deuterated ethylenes, depending on the relative rates of metathesis *versus* exchange. The pairwise scheme is presented in Eq. (o) and (p).



(o)

(p)

The di-deuterated and tetra-deuterated bidentate bisolefin complexes produced according to Eq. (p) will then metathesize yielding cyclohexene and the respective ethylenes in accordance with Eq. (o).

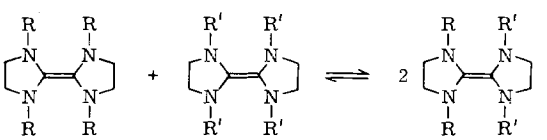
If intramolecular exchange were rapid and $k_{ex} \gg k_m$ (*i.e.*, the transalkylidenation step were rate determining), then one would expect a 1:0:1 distribution of [D_4]-, [D_2]- and [D_0]-ethylene in the initial stage of reaction. Thus, as a cyclohexene is displaced by a 1,7-octadiene [Eq. (o)] the new complex rapidly eliminates ethylene and forms a bidentate species [left

side of Eq. (p)]. If on the other hand $k_m \gg k_{ex}$, the resulting bisolefin complex would undergo transalkylidenation [right side of Eq. (p)], giving rise to the formation of some $CH_2{=}CD_2$ in addition to C_2H_4. *Grubbs* calculated 1:1.6:1 as being the limiting $[D_4]$-, $[D_2]$-, $[D_0]$-ethylene ratio for the process depicted in Eq. (o) and Eq. (p) when $k_m \gg k_{ex}$. Experimentally, the distribution was substantially different from either limiting value. The abundance of the respective ethylenes was closer to a statistical distribution, consistent with a non-pairwise mechanism. A significant finding was that the $[D_4]:[D_2]:[D_0]$ distribution of the residual 1,7-octadiene did not vary from start to finish in this particular metathesis experiment. This strongly indicates that essentially no regenerative intermolecular scrambling of methylenes among terminal double bonds of diene molecules took place. Furthermore, examining the $[D_4]$-, $[D_2]$-, and $[D_0]$-ethylene distribution before and after spiking the reaction mixture with $[D_0]$-ethylene led *Grubbs* to conclude that no significant degree of scrambling among the ethylenes took place under the prevailing reaction conditions.

Heretofore, a discussion of four experimental observations, mentioned quite often as evidence for a non-pairwise scheme for the transalkylidenation step, has been presented. Of these, *Grubb*'s work[25] stands alone as the one that cannot be readily accounted for by pairwise schemes.

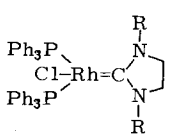
3. Evidence for Carbene-Metal Involvement

Although *Pettit*[6] did not apply "carbene" nomenclature to his pairwise transition state proposal, his description obviously alluded to an involvement of carbenes in olefin metathesis. Since then there have been several experimental disclosures that could be interpreted as providing evidence for carbene involvement in the reaction. *Cardin*[26] observed some disproportionation when he reacted a mixture of unsaturated amines with a rhodium phosphane catalyst [Eq. (q); $R = C_6H_5$, $R' = p\text{-}CH_3\text{—}C_6H_4$].



(q)

As a side product, a rhodium(I) complex with one half of the electron-rich olefin was isolated, for which the structure *(8)* was proposed. (The analogous compound with R′ instead of R has also been found.)



(8)

O'Neill[27] observed that a CoO/MoO_3 supported catalyst, which is active in propylene metathesis, readily decomposed diazomethane into ethylene and N_2:

$$2CH_2N_2 \rightarrow CH_2{=}CH_2 + 2N_2 \qquad (r)$$

It was suggested that the same sites that are active in metathesis "also selectively convert adsorbed methylenes into ethylene". Subsequently, *O'Neill*[28] demonstrated in an elegant fashion that a $Mo(CO)_6/Al_2O_3$ catalyst was capable of converting ethylene into propylene directly:

$$3CH_2{=}CH_2 \rightarrow 2CH_3CH{=}CH_2 \qquad (s)$$

O'Neill attempted to outline a mechanism for this unique $3C_2 \rightarrow 2C_3$ process. The suggested most "straightforward pathway" involved a splitting of one ethylene into methylenes, and addition of each of the latter to another ethylene, followed by rearrangement of the resulting trimethylene into propylene. It must be stressed that, although the catalyst for this process is formally a metathesis catalyst, the two reactions are qualitatively distinct. Any conceivable mechanism for the $3C_2 \rightarrow 2C_3$ reaction must reconcile migration of hydrogens. Selective olefin metathesis reactions do not involve hydrogen migrations. Hence, a carbene mechanism for a $3C_2 \rightarrow 2C_3$ cannot be reasonably "transplanted" to olefin metathesis.

Dolgoplosk[8] was able to demonstrate that an active catalyst for cycloolefin metathesis can be generated by co-reacting WCl_6 or WCl_4 with phenyldiazomethane. In the absence of cycloolefin monomer, a reaction analogous to *O'Neill*'s [Eq. (r)] was observed, and phenyldiazomethane was decomposed to nitrogen and stilbene. *Dolgoplosk* proposed a sequence as depicted in Eq. (t):

$$C_6H_5CH{=}WX_n + C_6H_5CHN_2 \rightarrow N_2 + C_6H_5CH{=}CHC_6H_5 + WX_n \qquad (t)$$

In the presence of cycloolefin monomer a very high molecular weight polyalkenamer is formed. The mechanism adopted for this polymerization is identical to *Chauvin*'s, wherein propagation-depropagation equilibrium [Eq. (e)] occurs at an active carbene-metal chain-end.

Recently, *Casey*[29] isolated $(C_6H_5)_2C{=}W(CO)_5$, a carbene-metal complex free of a heteroatom bonded to $C_{carbene}$. Until this report, it was generally believed that stable metal-carbene complexes required an electron donor heteroatom directly attached to the $C_{carbene}$. Following *Casey*'s work, *Schrock*[30,31] demonstrated that "unstabilized" carbene complexes of tantalum, such as $(CH_3)_3CHC{=}Ta[CH_2C(CH_3)_3]_3$ and $H_2C{=}Ta(C_5H_5)_2(CH_3)$, can be prepared, isolated and characterized.

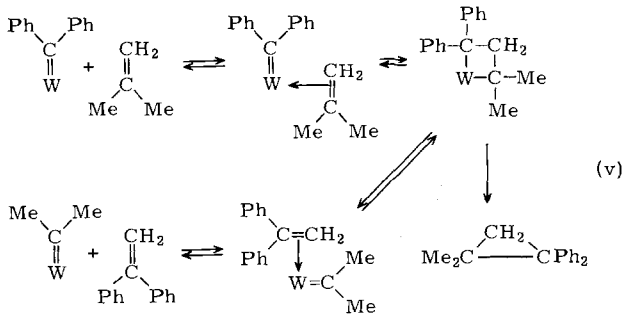
Upon heating $(C_6H_5)_2C{=}W(CO)_5$ with isobutene (100 °C, 2 h) a mixture of products was obtained[32], indicating a net transfer of a $[CH_2]$ group from isobutene to the diphenylcarbene [Eq. (u)].

$$(C_6H_5)_2C{=}W(CO)_5 + (CH_3)_2C{=}CH_2 \longrightarrow$$

$$(CH_3)_2C\overset{CH_2}{\text{———}}C(C_6H_5)_2 + (C_6H_5)_2C{=}CH_2 + W(CO)_5 \qquad (u)$$

The mechanism proposed for this reaction [Eq. (v)] accommodates both the observed cyclopropanation and the methylene transfer from isobutene to the diphenylcarbene (the carbonyl ligands have been omitted).

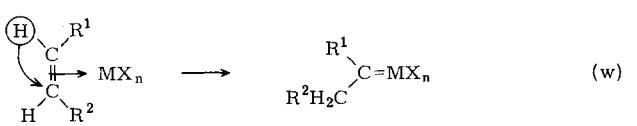
Casey's remarkable experiment, when first carried out, was stoichiometric rather than truly catalytic, and the element of reversibility was lacking. Very recently *Katz*[43] has shown that $(C_6H_5)_2C{=}W(CO)_5$ can in fact act as a metathesis catalyst.



(v)

4. Possible Origins of Carbene-Metal Species

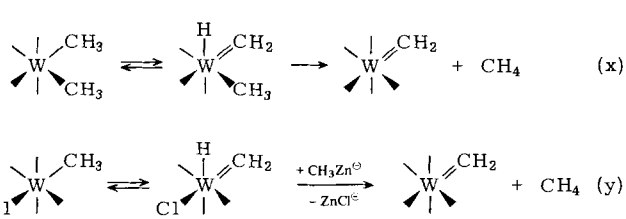
The variety of metals and their derivatives and combinations which demonstrate metathesis activity is very broad. If the non-pairwise carbene-to-metallocycle mechanism is to be accepted, it becomes of interest to examine potential routes to the formation of the initial carbene-metal entity. For this purpose it is convenient to classify metathesis catalysts into two major categories: a) catalyst combinations that do not involve an organometallic component, and b) combinations that involve organometallic cocatalysts. To the first category belong the classical heterogeneous supported catalysts such as MoO_3, $W(CO)_6$, and Re_2O_7 on alumina. Combinations such as WCl_6/AlX_3, or the photochemically induced $W(CO)_6/CCl_4$ which was recently disclosed independently by two research groups[34, 35], are also included in this category. Typical systems belonging to the second category are unmodified and alcohol-modified WCl_6/R_mAlCl_n $(m+n=3)$, $MoCl_5/R_3Al$, WCl_6/R_4Sn, $Mo[(Ph_3P)_2Cl_2(NO)_2]/R_3Al_2Cl_3$ and WCl_6/R_2Zn. As pointed out by *Dolgoplosk*[8], one may speculate that active catalysts of the first category undergo initiation, or in other words produce the original carbene-metal complex, by a process analogous to the one proposed by *Clark*[33], where a methoxycarbene-platinum entity was detected when certain acetylene-platinum complexes were reacted with methanol. The analogous transformation of an olefin-metal is illustrated schematically in Eq. (w).



(w)

It must be emphasized that this proposal is highly speculative, and no experimental evidence exists at present in support of such a process in actual metathesis reactions.

Catalyst systems that are activated by organometallic cocatalysts, presumably forming transition metal intermediates containing at least one alkyl group which is σ-bonded to the metal, are prone to transform into carbene-metal entities. *Muetterties*[36, 37] observed that, during the reaction of WCl_6 with metal alkyls, a significant evolution of alkanes takes



(x)

(y)

place. For example, in the reaction of $(CH_3)_2Zn$ with WCl_6 carried out in a deuterated solvent, methane free of deuterium was produced. It has been proposed that α-hydrogen elimination from the tungsten-methyl group occurs [Eq. (x) or (y)], leading to the formation of the initial carbene-tungsten complex.

The existence of a $W—CH_3 \rightleftarrows W(=CH_2)H$ equilibrium, proceeding by migration of an α-hydrogen from a σ-bonded alkyl to the metal, has also been proposed by *Green*[38] in connection with the reversible rearrangement [Eq. (z)]:

$$[W(C_5H_5)_2(PR_3)CD_3]^{\oplus} \rightleftharpoons [W(C_5H_5)_2(CD_2PR_3)D]^{\oplus} \qquad (z)$$

Recent work by *Schrock* with organotantalum compounds suggests the feasibility of both intramolecular and intermolecular α-hydrogen abstractions as straight-forward routes to isolable carbene-tantalum complexes which are not stabilized by a heteroatom. X-ray and NMR analyses were employed[39] to determine the structure of $CH_2=Ta(C_5H_5)_2CH_3$ and to estimate the energy barrier to rotation about the $Ta=CH_2$ double bond. The complex, as illustrated in Fig. 2, has two eclipsed cyclopentadiene rings. The $H_2C—Ta$ bond length is shorter than the $H_3C—Ta$ bond, indicating some double bond character for the methylene ligand. The methylene ligand is oriented perpendicular to the C—Ta—C plane. These observations are in accord with the concept of a $C_{carbene}$ having an sp^2 hybridization, wherein its vacant p_z orbital can overlap preferably with a hybridized Ta orbital in the C—Ta—C plane.

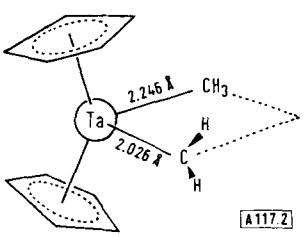


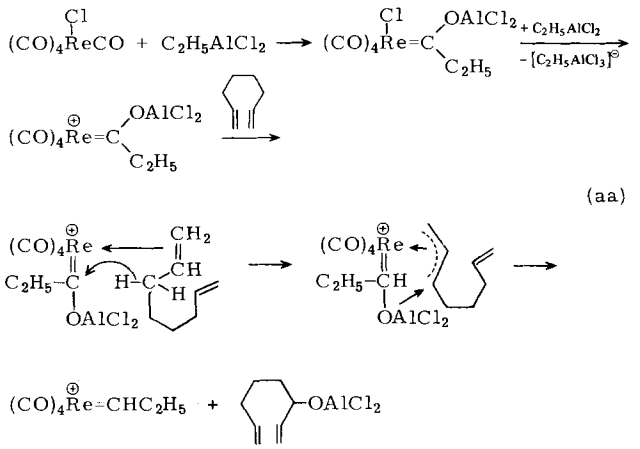
Fig. 2. Structure of the complex $CH_2=Ta(C_5H_5)_2CH_3$.

The barriers of rotation for $=CH_2$, $=CHC(CH_3)_3$, and $=CHC_6H_5$ around the respective $C_{carbene}—Ta$ bonds were estimated from temperature-dependent NMR analyses[39]; the free energies of rotations, $\Delta G^{\neq}$, are ≥ 21.4, 16.8, and 19.3 kcal/mol for the respective carbene ligands. These high values directly reflect the significant double bond character of carbene-metal complexes that bear no heteroatom substituents on the carbene carbon atom.

Evidence for an alternate route for the formation of the original carbene-metal entity was submitted recently by *Farona*[40, 41]. Using $Re(CO)_5Cl$ in combination with either $C_2H_5AlCl_2$ or CH_3AlCl_2, the homo-metatheses of 1,7-octadiene and 4-octene was investigated. Using highly sensitive GC-Mass Spectroscopy techniques, he was able to monitor trace amounts of anomalous olefinic products which were proposed as resulting from the first-formed carbene. The first-formed olefins in the metathesis of 1,7-octadiene when $C_2H_5AlCl_2$ cocatalyst was employed were identified as 1-butene and 1,7-decadiene, whereas when 4-octene substrate was used, minute amounts of 3-heptene were found. Accordingly, *Farona* concluded that the original carbene-metal must have been a propylidene-Re entity. In an analogous experiment

using CH_3AlCl_2 cocatalyst, the first-formed olefins suggested the formation of an ethylidene-Re carbene initially.

The proposed mode of formation of the original propylidene-Re complex as postulated by *Farona*[41] is illustrated in Eq. (a, a):



(aa)

The presence of an unusual by-product, octa-1,7-dien-3-one, was claimed as supporting evidence for this scheme.

In conclusion, whereas formation of the original carbene-metal can be explained in catalyst systems that involve metal alkyl components, no experimental work exists to suggest a pathway for carbene formation in catalyst systems that do not employ organometallics. Evidence supports the contention that sp^2-bonding of carbene ligands which are not stabilized by heteroatom substituents is substantial, and the carbene-metal bond should be viewed as a double bond in the proposed carbene-to-metallocycle mechanism.

5. Structural Selectivity in Cross-Metathesis Reactions

Earlier, we disclosed[17, 18, 20] that certain catalysts which display a low apparent metathesis activity with terminal olefins, when employed on mixtures of terminal and internal olefins, lead to the selective formation of cross metathesis products. Table 2 presents the relative distribution of the various cross metathesis products of 1-pentene with *cis*-2-pentene after 25% of the original 2-pentene had been consumed (50% of theoretical equilibrium). Self-metathesis of either olefin will lead to symmetric products; ethylene and 4-octene from 1-pentene, and 2-butene and 3-hexene from 2-pentene. The major products from the cross metathesis were the unsymmetric ones. Depending on the orientation of the incoming olefin with relation to a specific carbene-metal site, one can obtain propylene, 3-heptene, 1-butene and 2-hexene. The data point to the fact that, although 1-pentene is sluggish towards self-metathesis, it readily reacts with 2-pentene to produce the unsymmetric cross products. The results also suggest that 1-pentene, in fact, inhibits the self-metathesis of 2-pentene to the extent that the tendency of 2-pentene to yield cross products with 1-pentene is eight times greater than its tendency to self-metathesize. This observation was recently reconfirmed by *Muetterties*[42] using a $RAlCl_2/WCl_6/ROH$ catalyst on 2-pentene and 1-nonene substrates. A possible hypothesis for this observation is that terminal olefins are, in fact, *more* reactive than internal olefins, but that they prefer to undergo regenerative metathesis *via* either metallocycle *(9)* or *(10)*.

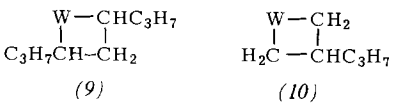
Table 2. Cross metathesis of 1-pentene and *cis*-2-pentene (after Ref. [18]).

$C_3H_7{=}CH_2 + C_2H_5CH{=}CHCH_3$

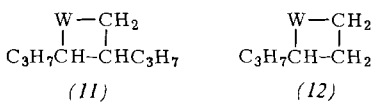
Relative concentrations [a]			
Symmetric		Unsymmetric	
$CH_2{=}CH_2$	1	$CH_3CH{=}CH_2$	4
$C_3H_7CH{=}CHC_3H_7$	1	$C_2H_5CH{=}CHC_3H_7$	4
$CH_3CH{=}CHCH_3$	2	$C_2H_5CH{=}CH_2$	12
$C_2H_5CH{=}CHC_2H_5$	2	$CH_3CH{=}CHC_3H_7$	12

[a] Values at 50% of theoretical equilibrium.

This phenomenon has been recently reconfirmed by *Katz*[43] and *Muetterties*[42]. Evidently, transition states *(11)* and *(12)* are not favored, since they are incompatible with regenerative metathesis.



(9) *(10)*



(11) *(12)*

When terminal and internal olefins are co-reacted, regenerative metathesis prevails, thus inhibiting self-metathesis of the internal olefin. Terminal olefins occupy the catalyst, but occassionally an internal olefin enters the complex, whereupon metathesis yields an unsymmetric product.

The regenerative methathesis of terminal olefins was confirmed experimentally by examining the product distribution in the cross metathesis of 1-pentene with $[D_{10}]$-1-pentene (Table 3).

Table 3. Cross metathesis of 1-pentene and $[D_{10}]$-1-pentene; GC/MS data. C_8H_{16}, $C_8H_8D_8$ and C_8D_{16} formed only in trace amounts (after Ref. [18]).

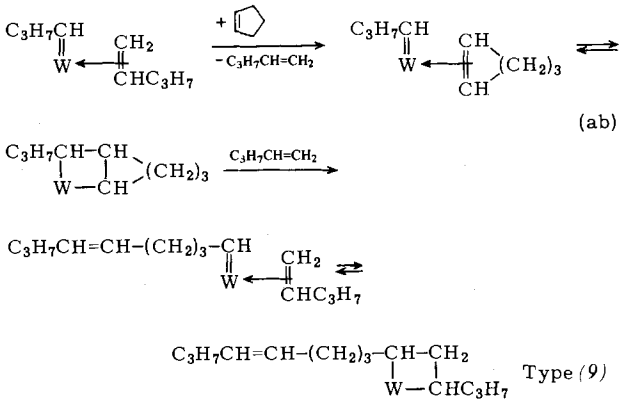
Compounds	*m/e*	Relative concentrations initially	after 10 min	equilibrium (calc.)
$C_3D_7CD{=}CD_2$	80	0.1074	0.0395	0.0115
$C_3D_7CD{=}CH_2$	78	—	0.0685	0.0959
$C_3H_7CH{=}CD_2$	72	—	0.0771	0.0959
$C_3H_7CH{=}CH_2$	70	0.8926	0.8148	0.7967

The data in Table 3 indicate that after a 10 minutes' reaction the original mixture of $C_3H_7CH{=}CH_2$ ($m/e=70$) and $C_3D_7CD{=}CD_2$ ($m/e=80$) underwent about 70% of the theoretical scrambling. Only trace amounts of 4-octenes were formed.

In an attempt to resolve whether regenerative metathesis of terminal olefins proceeds *via* transition state *(9)* or *(10)*, the route of telomer formation was examined in the cross metathesis of 1-pentene and cyclopentene. This has been reported[18, 20] to produce preferentially the homologous series of unsymmetric polyenes of the general formula $C_3H_7CH[{=}CH{-}(CH_2)_3{-}CH{=}]_xCH_2$ (C_{10}, C_{15}, C_{20}...*etc.*), along with minor amounts of the two symmetric homologous series, $CH_2[{=}CH{-}(CH_2)_3{-}CH{=}]_xCH_2$

(C_7, C_{12}, C_{17}, C_{22} *etc.*) and $C_3H_7CH[=CH-(CH_2)_3-CH=]_xCHC_3H_7$ (C_{13}, C_{18}, C_{23}, C_{28} *etc.*)[*]. Figure 3 shows a chromatogram of a [1-pentene + cyclopentene] reaction product mixture. The main peaks are attributed to the unsymmetric homologous compounds.

If regenerative metathesis were to proceed *via* intermediate *(9)*, it is evident that the eventual incorporation of cyclopentene units to form the unsymmetric polyenes will follow sequence (ab):



(ab)

On the other hand, if one assumes that the regenerative metathesis of 1-pentene proceeds *via* transition state *(10)*, then an accounting of the production of the selective unsymmetric polyenes will require the participation of an "unfavored" transition state of type *(11)* [see Eq. (ac)].

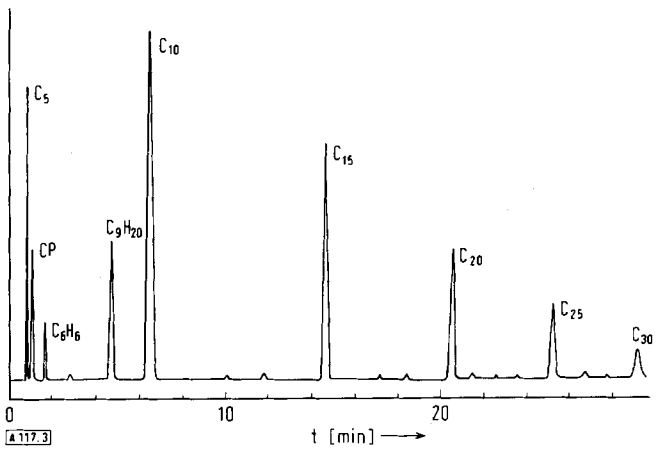
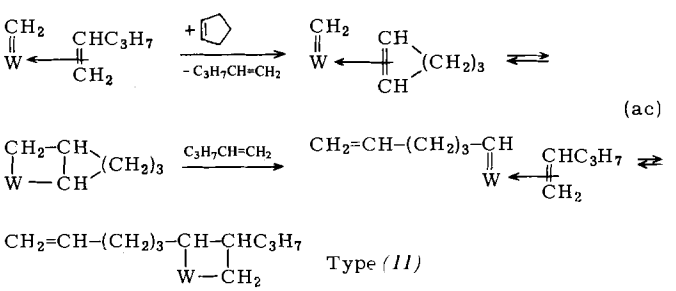


Fig. 3. Gas chromatogram of polyenes obtained in the 1-pentene + cyclopentene cross metathesis (after Ref. [18]).



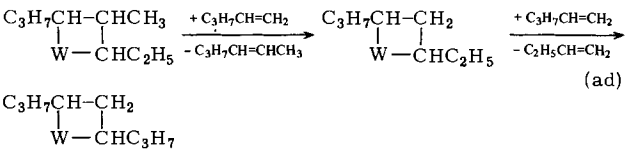
(ac)

[*] In reactions of cyclooctene with α-olefins. *Herisson* and *Chauvin* also found high selectivity at low conversions [11], although a lesser selectivity was observed by *Lal* and *Smith* at higher conversions of the cyclooctene [48].

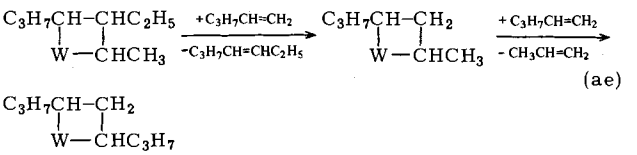
Since two types of carbenes are invoked here, the course of reaction in Eq. (ac) may be energetically less favorable than that of Eq. (ab), which invokes entirely monosubstituted carbenes throughout. However, the results do not unequivocally exclude either scheme.

Studies involving cross-reactions of ethylene with internal olefins might be of value, since types *(11)* and *(12)* would now be unavoidable during the formation of cross-products, and kinetic effects might become discernible.

Some insight into the influence of steric effects on the course of metathesis reactions was revealed in the reaction of 1-pentene with 2-pentene discussed previously. For a reaction sequence analogous to that in Eq. (ab), cross-metathesis would be preceded by formation of $C_3H_7CH{=}W(CH_3CH{=}CHC_2H_5)$, which is capable of yielding two isomeric metallocycle intermediates. These will subsequently afford either 2-hexene and 1-butene [Eq. (ad)] or 3-heptene and propylene [Eq. (ae)].



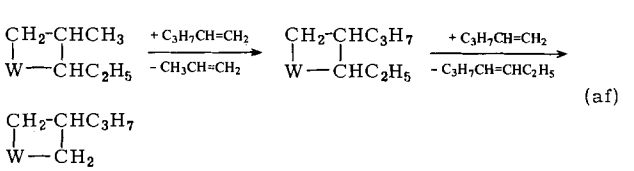
(ad)



(ae)

The data in Table 2 suggests that, for the catalyst system $(C_2H_5)_2AlCl/WCl_6/ClC_2H_4OH$, reaction sequence (ad) is significantly favored over that of (ae). One must attribute this difference in ease of formation of the respective products to steric hindrance. On the basis of reaction scheme (ae), the implication appears to be that steric interactions involving substituents located on the β-carbon in the transient metallocycle ring are more severe than those for the α-carbon substituents, although the origin of this steric demand is not obvious.

Further evidence for preferential formation of a metallocycle where the least substituted carbon is preferentially the β-carbon was given recently by *Casey*[32, 44]. In model compound studies involving a tungsten compound which contained a bulky diarylcarbene ligand, transfer of an alkylidene unit from a reacting olefin resulted in highly selective transfer of the least substituted alkylidene unit, as described previously in Eq. (v). The authors pointed out that the new metal-carbene species which resulted after metathesis was preferentially that



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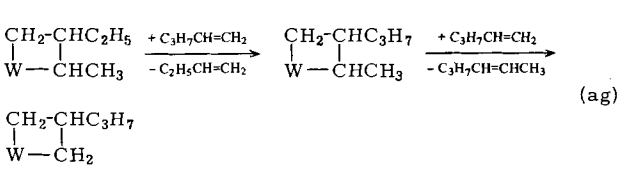

(ag)

which possessed the most stable (*i.e.*, highly substituted) carbene.

In considering the steric effects observed in the reaction of 1-pentene with 2-pentene, one can also invoke a scheme which evolves from structure *(9)* [analogous to Eq. (ac)].

The product distribution in Table 2 now indicates pathway (ag) to predominate, and is consistent with the notion that the greatest steric interactions occur nearest the transition metal. Here, crowding due to adjacent ligands about the metal would appear to be a plausible source of these steric effects.

6. Conclusions

Despite numerous new and sophisticated experiments continually being brought to bear on questions regarding the chemistry of olefin metathesis, a number of challenging problems remain unsolved.

The concensus of recent publications is that a chain process, presumably involving a metal-carbene species, is operating, yet arguments in support of the pairwise scheme continue to rise Phoenix-like. Most recently, *Gassman*[45] presented new data to show that, with an appropriately chosen diolefin, quantitative interconversion of the diolefin to a cyclobutane structure could be accomplished using a typical olefin metathesis catalyst. Previously, the failure to observe cyclobutanes during metathesis reactions had been given as one argument against the plausibility of the "quasicyclobutane" transition state. It had been expected that, since two isolated double bonds are energetically comparable to a cyclobutane, both forms should be present under metathesis conditions according to the pairwise scheme. *Gassman* points out that the determining factor may be the relative energies of a pair of coordinated double bonds (substantial stabilization) *vs* a coordinated cyclobutane (very little stabilization), rather than the relative stabilities of the free species.

Mechanisms invoking other intermediates such as the tetrahedral trimethylene model (where all three methylenes are equally related to the metal), as described by *Haines* and *Leigh* in their recent excellent and comprehensive review[46], may also adequately explain metathesis reactions, and cannot be discounted. In fact, several authors have suggested that perhaps more than one pathway for metathesis may be possible, and in a given situation would be determined by the type of catalyst used.

Because of the tremendous variety in reagents which serve to generate metathesis-active species, reconciliation of a common mechanism for metathesis in these diverse systems represent a real challenge. Certainly, the catalysts appear quite tolerant of diversity in ligands about the transition metal, with the possibility of bimetallic species being suggested occassionally.

The origin of stereospecificity in metathesis reactions remains a mystery. Homogeneous catalysts rather universally show a weak *cis*-directing tendency in the reaction of *cis*-olefins. *Basset*[47] demonstrated that regardless of the catalyst used, *cis*-2-pentene afforded about 55 % *cis*-3-hexene and 60 % *cis*-2-butene initially. When cycloolefins are employed, however, wide variations in polymer structure are known to occur, depending upon the catalyst used. Apparently the growing polymer chain exerts a pronounced influence on the stereospecificity of the metathesis process. This phenomenon may be due to multiple coordination of the polymer chain, which cannot occur in the reaction of acyclic olefins.

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Chemotherapy of Virus Diseases

By Guy D. Diana and Francis Pancic[*]

The purpose of this review is to provide an overview of current screening methodology and major advances in the area of viral chemotherapy. This presentation will be limited to those drugs which are currently in use and those which having shown activity against major human pathogenic viruses are now being evaluated in man.

1. Introduction

Over the past several years, antiviral chemotherapy has presented a major challenge to medical science. Although numerous antiviral compounds have been reported from experimental screening programs, only a few have been studied clinically and even fewer have become commercially available drugs.

The need for a broad spectrum antiviral agent is pressing, but it would appear that the possibility of finding such a drug is rather remote. Most currently available drugs or those in clinical trials are effective against only specific viruses and, in some cases, against only one particular strain in a group of viruses. Despite these problems, the search for effective antivirals is continuing.

The mechanism of viral replication suggests several points of attack for selective inhibition. The structure of the virus consists of an inner core of nucleic acid surrounded by a protein coat. Viral replication can only take place inside the host cell where the virus uncoats and enters an eclipse phase. This is followed by the replication stage where new nucleic acid is synthesized, and coated with protein, at which point the new virus is released from the cell. An antiviral agent may work directly on the virus particle itself, prevent entry of the virus into the host cell, interfere with the uncoating process, inhibit viral replication, or interfere with the synthesis of the protein coat.

Viral chemotherapy is a quest for selective toxicity. A drug which interferes with viral DNA, RNA, or protein synthesis quite often affects analogous elements of the host cell as well. The requirement of achieving selective toxicity complicates the search for new antiviral agents by the currently available screening methods.

Although many viral diseases such as the common cold (rhinovirus) are self-limiting with a low mortality and high morbidity, they cause much discomfort to the individual and represent millions of lost hours with serious economic repercussions. A drug which would prevent, cure, or shorten the duration of these illnesses would be welcomed.

50 to 75 % of the adult population throughout the world suffers from some form of mucocutaneous lesions produced by herpes virus[1]. In addition, the same group of viruses are responsible for more serious illnesses such as herpetic encephalitis and keratoconjunctivitis.

The incidence of herpes progenitalis in man has increased significantly in recent years and may be considered as one of the most common types of venereal disease.

2. Screening Methodology

Several methods are available for screening compounds *in vitro* for antiviral activity, one of which is described in this review.

Since viruses replicate only in living cells, it is necessary to propagate human or animal tissue cells *in vitro* which will be a suitable host for specific viruses. Such a system of growing and propagating cells *in vitro* is known as cell or tissue culture. Primary tissue cultures are monolayers of dispersed cells which are derived from a freshly removed organ and grown in a sterile synthetic nutrient medium containing a complex mixture of amino acids, inorganic salts and often animal blood serum. Cells grow attached to the surface of a sterile glass or plastic vessel.

When the cells from a primary culture are adapted by numerous successive passages to grow indefinitely *in vitro*, they are referred to as cell strains or continuous cell lines. Many such cell strains and lines have been propagated for years in various laboratories, and an initial screening of potential antiviral drugs is commonly carried out in such systems.

When the virus is introduced into a monolayer of susceptible tissue culture cells, it becomes intracellular, replicates as described previously, and proceeds to destroy the cells. This cellular destruction is observed microscopically and is termed the "cytopathic effect" (CPE).

The addition of potentially active antiviral substances shortly after the virus is allowed to adsorb onto the cells may prevent virus replication and inhibit viral CPE. Any compound indicating activity against a given virus is then further examined *in vitro* to determine whether the activity is limited or has broad antiviral potential.

Active compounds are then evaluated in an *in vivo* model to confirm activity. For the *in vivo* evaluation, numerous animal models are available. For example, influenza viruses readily grow in the respiratory tract of mice or ferrets. Herpesvirus grows in various organs of rabbits, guinea pigs, mice, *etc.*

Local or systemic infections can often be produced and various parameters are used to evaluate efficacy and potency; survival of the animal, reduction of the severity of the symptoms, and titer of the virus in treated *versus* placebo animals are the most common criteria.

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The animal experiment as well as the mode of therapy must be designed in such a way to mimic the human condition as closely as possible.

3. The Current Status of Antiviral Chemotherapy in Man

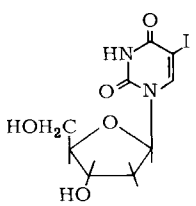
3.1. Herpesvirus

One of the most ubiquitous viral agents in man is Herpes simplex (type 1 and 2), which causes a variety of clinical conditions ranging from the familiar fever blister (herpes labialis) to life-threatening situations arising from herpes encephalitis. The virus usually establishes itself in many sites of the body such as the mouth, genitals, skin, eyes, and nerve tissue and may be reactivated from its latent state after the host is stressed by such things as exposure to sunlight, physical stress, menstrual cycle, or therapy which suppresses the immune system.

3.1.1. 5-Iodo-2'-deoxyuridine (IUDR)

Although herpetic keratoconjunctivitis is not as prevalent as herpes labialis, it is the most crippling disease of the eye and one of the major causes of blindness in the USA. Once present in an individual the disease is hard to eradicate. Relapses of the infection are common with progressively increased ocular damage resulting.

One of the first successful antiviral agents that became a useful drug for the treatment of herpetic keratitis is 5-iodo-2'-deoxyuridine *(1)*, the synthesis of which was first reported by *Prusoff*[2], who studied its effect on microbial growth.



(1), IUDR

It was also found that IUDR reversibly inhibited the cellular utilization of thymine-containing precursors of DNA-thymine. *Herrmann*[3] examined the effect of IUDR on the plaque formation by vaccinia and Herpes simplex viruses. In this test IUDR proved to be a potent viral inhibitor. The corresponding bromo and fluoro homologs were found to be inactive. IUDR was subsequently tested topically against Herpes simplex and vaccinia viruses by *Kaufman*[4], who found the drug to be very effective against herpetic corneal infections. Further clinical studies substantiated the efficacy of IUDR against herpes keratitis. Currently, it is the only commercially available drug for the treatment of this disease.

In the years since the introduction of IUDR, a number of limitations of the drug have been pointed out. It is active chiefly in superficial epithelial keratitis and is not very effective in deeper stromal infections[5]. IUDR inhibits viral DNA synthesis, but it also inhibits host cell DNA replication, with potential for cellular damage on prolonged administration. It does not eradicate the infection completely from the eye and recurrence is not uncommon. Resistant strains of virus have been isolated from patients who did not respond to IUDR treatment[6].

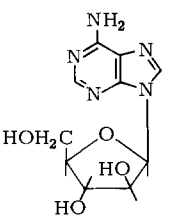
IUDR was ineffective against cutaneous herpes when applied as an ointment or in polyvinyl alcohol on lesions of the face[7]. Other studies, however, indicated that when IUDR was applied as a DMSO solution, the duration of the disease was shortened by 63 % when compared to untreated placebo controls[8].

Herpetic encephalitis is a viral encephalitis found in man, affecting children most often. Although IUDR was tried systemically in numerous cases, there is no clear evidence available that drug treatment significantly influenced the course of the disease[9]. Intravenous administration produced side effects such as thrombocytopenia, leucopenia, and bone marrow depression[10].

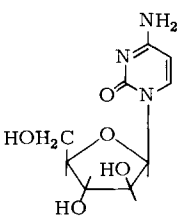
IUDR was reported effective against varicella-zoster (shingles) when it was applied topically as a 40 % DMSO solution[11].

3.1.2. Adenine Arabinoside (Ara-A) and Cytosine Arabinoside (Ara-C)

Two other nucleosides have shown promise as antiviral agents particularly against herpes keratitis—Ara-A *(2)* and Ara-C *(3)*. Ara-A was first synthesized by *Lee*[12] as a potential



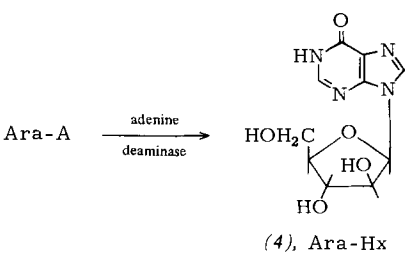
(2), Ara-A



(3), Ara-C

anticancer agent *via* its inhibition of DNA synthesis. Some antitumor activity was observed but it was not considered for this type of therapy. Ara-A was later found active *in vitro* against Herpes simplex virus and vaccinia virus[13], and against cytomegalovirus *in vitro*[14] and *in vivo*[15]. In addition to the broad spectrum of activity *in vitro* against DNA viruses, activity *in vivo* in hamsters was observed against herpes keratitis, intracerebrally innoculated Herpes simplex, and vaccinia virus in mice[16].

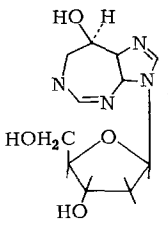
Ara-A is enzymatically converted to 1-β-D-arabinofuranosyl hypoxanthine (Ara-Hx) *(4)* by adenine deaminase. This metabolite has antiviral properties. Recently, it was reported that small quantities of an adenine deaminase inhibitor, Co-vidarabine *(5)*, when administered subcutaneously enhances the



(4), Ara-Hx

in vivo activity of Ara-A against Herpes simplex in mice by a factor of 10 as measured by the number of survivors[17]. No activity was demonstrated when this combination was given orally. Ara-A has exhibited activity against herpes keratitis in man[18].

In the treatment of epithelial keratitis, Ara-A is similar to IUDR with respect to the rapidity of activity. However, in deeper stromal infections, its effectiveness is less certain. Ara-A is recommended for use in patients sensitive or refractory to IUDR treatment or as an alternate to the latter in recurrent keratitis. The drug is reported to be less toxic than IUDR to the corneal epithelium, which is of major significance when the treatment must be extended for a prolonged period of time[19].



(5)

The topical efficacy of Ara-A in herpes progenitalis has not been as well documented as its activity in the eye. In a double blind study, topical administration of Ara-A did not modify the course of the disease in man[20].

In the cutaneous or genital treatment, it is apparent that the drug must be delivered in a suitable vehicle to reach the site of virus replication. Thus, the tissue penetration by the drug plays an essential part in its efficacy.

Ara-A is being evaluated in man in cases of herpetic encephalitis, varicella-zoster, cytomegalovirus disease as well as mucocutaneous herpetic infections. Although none of the studies have reported definitive efficacy of Ara-A treatment, there is some evidence of a favorable response. In systemic treatment, Ara-A must be administered intravenously as an infusion, requiring a large daily fluid intake[21]. Since Ara-A has been found to be teratogenic in rats and rabbits[22, 23], systemic treatment is limited to either life-threatening diseases or those that produce severe disability. At the moment there are 22 centers participating in double blind evaluations of the efficacy of Ara-A in systemic therapy[24].

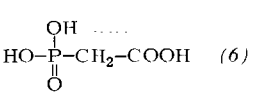
Ara-A[25–30] appears to inhibit DNA polymerase and/or ribonucleotide reductase. However, further studies are required to fully define the mode of action.

Ara-C *(3)* has a spectrum of antiviral activity similar to Ara-A. It is active *in vitro* against DNA viruses (herpesvirus, varicella-zoster, cytomegaloviruses and vaccinia virus)[31] and is clinically useful in the treatment of granulomatic leukemias.

The prospect that Ara-C might be useful in the treatment of disorders caused by varicella-zoster led to the first clinical trial with disseminated zoster[32], a serious disease that develops in immunologically suppressed patients. The condition is often manifest in organ transplant cases or in cancer patients undergoing drug chemotherapy. Unfortunately, Ara-C was not effective in the systemic treatment of this condition and toxicity was evident.

3.1.3. Disodium Phosphonoacetate

Phosphonoacetic acid *(6)*, which has been known for over 50 years, was discovered to have antiviral activity against herpes 1 and 2 when screened *in vitro*[33]. *In vivo* studies on corneal HSV infections in the rabbit, showed that 5% phosphonoacetic acid prepared as the disodium salt, suppressed the herpes keratitis in laboratory animals[34]. It has also been found effective in mice against herpes virus infections of the CNS when administered by intraperitoneal injections[35]. The drug appears to act by blocking DNA-dependent DNA polymerase[36, 37].



(6)

3.2. Human Respiratory Viruses

One of the most prevalent group of viruses are those that affect the upper and lower respiratory tract. Viruses in this class usually produce a low mortality but high morbidity, as for example, the common cold. Influenza, parainfluenza, rhinovirus, respiratory syncytial virus, and adenovirus are not, at the present time, under chemotherapeutic control. Influenza viruses invade both upper and lower respiratory tracts and are responsible for diseases of epidemic proportions. Potentially, influenza may lead to death particularly in individuals with impaired respiratory or circulatory functions. Respiratory syncytial virus which affects the lower respiratory system occurs mainly in the very young where 80% of the reported cases in one study were in the group aged 0—4 years[38]. It has been associated with bronchitis and pneumonia in this age group. Adenovirus also affects the very young but not to the extent of respiratory syncytial virus and manifests itself in a wide range of clinical symptoms varying from skin lesions to gastrointestinal infections and even CNS disease. It is often seen among military recruits, assuming epidemic proportions in army camps.

3.2.1. 1-Aminoadamantane Hydrochloride (Amantadine Hydrochloride)

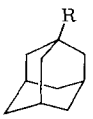
The discovery of the antiviral activity of 1-aminoadamantane *(7a)* against certain strains of influenza[39, 40] created considerable interest. Unfortunately, the spectrum of activity is rather narrow. Amantadine is active, particularly against the A2 strain of influenza, less effective against C strain, and inactive against the B strain.

In a mouse influenza model, where animals were infected intranasally with strain A2, oral or systemic administration of amantadine (25 to 50 mg/kg daily) prevented death in 90 to 100% of animals.

In man, the efficacy of amantadine was demonstrated in controlled clinical trials[41–43]. The drug is most effective when given prophylactically at the time of infection or in the early phase of the disease, where it was shown to be of value in preventing the A2 influenza infection. Therapeutically, it was reported to shorten the course of the disease, reduce the severity of clinical symptoms and shorten the time and duration of fever.

Rimantadine *(7b)*, a homologue of amantadine, in addition to being more active *in vitro* was reported to inhibit other RNA viruses such as rubella, rubeola, respiratory syncytial, and parainfluenza viruses *in vitro*[44].

Numerous modifications have been made in the adamantane structure. *Swallow*[45] found good activity against influenza A2 when an ionizable group was present [as in *(7c)* to *(7e)*] but that activity was considerably reduced with the introduction of a nonionizable group [as in *(7f)* and *(7g)*]. *Schlat-*



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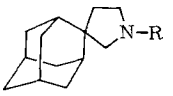


(8)

(7a), R = $NH_2 \cdot HCl$

(7b), R = $CH(CH_3)-NH_2 \cdot HCl$

(7c), R = NH_2

(7d), R = CH_2-NH_2

(7e), R = COOH

(7f), R = $NH-CO-CH_3$

(7g), R = $CO-NH_2$

(7h), R = $NH-CO-NH_2$

(7i), R = $NH-C(=NH)-NH_2$

(7j), R = $NH-C(=NH)-NH-C(=NH)-NH_2$

mann[46] reported that the urea, guanidine, and biguanide derivatives [*(7h)*, *(7i)*, and *(7j)*, respectively] all exhibited activity comparable to amantadine *in vitro*. However, *in vivo* the activity was diminished and undesirable side effects were observed.

In a series of adamantane spiro compounds *(8)*[47], the *N*-methyl derivative was three times more active *in vivo* against influenza A2 Japan and A2 Hong Kong than amantadine *(7a)*. A broader spectrum of activity was observed *in vitro* which included activity against Coxsackie A21 and Rhino 2 (HGP).

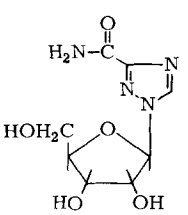
Amantadine is reported to exert its effect in the early phase of viral replication, affecting the penetration of virus into the host cell[48–50]. The virus appears to bind to the surface of the cells in the presence of the drug. The drug does not have virucidal activity outside the host cell.

Some side effects were noted with the administration of amantadine such as mild gastrointestinal irritation and some sporadic central nervous system reactions[51, 52].

Rimantadine *(7b)* as well as spiroadamantane *(8)*, R = CH_3, are currently being evaluated further.

3.2.2 Virazole (Ribavirin)

Virazole *(9)*, a broad spectrum antiviral agent, was synthesized by *Simon et al.*[53] and found effective against both DNA and RNA viruses[54, 55]. Most recently, virazole when administered to mice was 90% effective against influenza[56]. Mode of action studies suggested that the antiviral effect may be the result of an inhibition of GMP synthesis at the step involving the conversion of IMP to XMP.



(9), Virazole

Virazole is currently available in South America where it has undergone clinical trials against influenza A2[57], viral hepatitis[58], and varicella-zoster[59]. In the USA a study at John Wesley County Hospital in Los Angeles indicated that virazole was ineffective against hepatitis B[60].

3.3. Interferon

Interferon is a low molecular weight protein produced in the body as a defense against viral infection. Cellular synthesis of interferon is stimulated by either viral antigen or by a chemical inducer. It is detectable in the blood stream and peak levels appear within 24 hours after infection. In terms of combating viral infection, natural body defense mechanisms would appear to be the ideal system. As a result, a considerable amount of work has been done clinically to study the effect of endogenous interferon in peventing or curing viral infections.

Merigan et al.[61] reported a statistically significant effect when interferon was administered intranasally one day prior to and three days postinfection to volunteers infected with rhinovirus. Treatment prevented the development of clinical symptoms and eliminated virus shedding. Other strains of rhinovirus were not tested but *in vitro* studies would suggest that they might respond favorably to exogenous interferon. *Came et al.*[62] reported the sensitivity *in vitro* of 20 human rhinoviruses to human interferon from two sources, human leucocytes, and human foreskin fibroblasts. They found that the sensitivity of various strains varied depending on the type of tissue culture used to grow the virus as well as on the source of the interferon. In one type of tissue culture a strain of rhinovirus was inhibited with 20 to 40 units, while a different type of the rhinovirus was not inhibited with 5000 units. However, when both viruses were grown in a different type of tissue culture, both were inhibited with relatively low concentrations (0.5 to 5.0 units of interferon).

Interferon was reported to exhibit some effect on the onset of rubella infections[63] when administered systemically beginning 7 h before vaccination. Another study demonstrated the effect of interferon on herpes zoster[64] when administered intramuscularly for 5 days at doses of 100000 units. Finally, 50000—100000 units of interferon was administered topically four times daily to the eye of a patient with IUDR resistant herpetic keratitis and, within 3 days, healing was observed[65].

3.4. Interferon Inducers

3.4.1. Polynucleotides

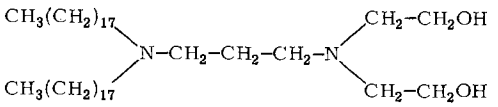
Poly(I,C) has been incorporated into a complex with poly-l-lysine and carboxymethyl cellulose, which is nuclease resistant, and presumably would improve the interferon induction capacity of this polynucleotide[66]. Promising results were obtained in monkeys against, among other viruses, yellow fever and rabies[67].

The stimulation of endogenous interferon by poly(I,C) has also been demonstrated *in vitro* and *in vivo*. The inducer was tested by intranasal administration in human volunteers starting one day prior to the infection by either rhinovirus type 13 or influenza A2[68]. A small but definite reduction of the clinical symptoms in the upper respiratory tract was recorded for drug treated patients. Some reduction of virus shedding was reported for rhinovirus but not for influenza virus.

Toxic effects of poly(I,C) appear to preclude its use in man other than for topical application[69–71].

3.4.2. *N,N*-Dioctadecyl-*N',N'*-bis(2-hydroxyethyl)-1,3-propanediamine

N,N-Dioctadecyl-*N',N'*-bis(2-hydroxyethyl)-1,3-propanediamine *(10)* was found active when administered to mice



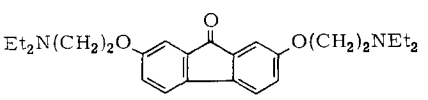
(10)

parenterally 6 to 12 h before infection. It provided protection against lethal infections of encephalomyocarditis and Semliki Forest virus and suppressed pock formation by vaccinia virus[72]. Clinical studies[73,74] substantiated the interferon induction previously seen in animal studies and further indicated that the drug provided protection against rhinovirus-induced disease. A double blind study using this propanediamine was conducted to determine the topical production of interferon by the local cells in the upper respiratory tract against rhinovirus infection. The inducer was administered intranasally starting one day prior to the virus infection. A high titer of interferon was reported in the nasal wash as compared to the placebo control, with decreased infectivity of the virus, reduced severity of the symptoms, and decreased virus shedding.

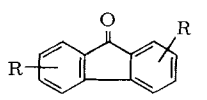
3.4.3. Tilorone

Probably one of the most interesting developments in the area of antiviral chemotherapy was the discovery that a non-polymeric compound 2,7-bis(2-diethylaminoethoxy)-9-fluorenone dihydrochloride *(11)* (tilorone hydrochloride) was able to induce high levels of interferon[75-80]. [Compound *(10)* was unknown at that time[72-74].]

A large number of homologs of *(11)* were prepared in order to establish a structure-activity relationship[81-86], the most effective compounds being the bis(aminoalkyl) esters *(12)* derived from fluorenone. Strongly basic amine functions appeared necessary as well as a C_3 chain separating O from N in the ester side chains. A study by *Kaufman et al.* demonstrated that tilorone failed to elicit detectable interferon in humans. Furthermore, toxicity was seen when the compound was administered either orally or topically. *Kaufman* concluded that even at high topical doses, tilorone hydrochloride is neither safe nor effective[87].



(11)
Tilorone



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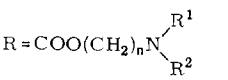


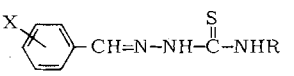
Preliminary clinical results confirm the efficacy of interferon as an antiviral agent. At the present time, however, several barriers stand in the way of its practical application. Interferon is species-specific which limits the source for clinical use. This leads to a second problem which is production of large quantities of human interferon. Technologically, at the present state of the art, it is not feasible to produce interferon on a commercial scale. Finally, the instability of interferon in body fluids requires doses which are probably well in excess of the effective level.

The use of interferon inducers, while attractive in overview, presents problems of toxicity and/or pyrogenicity in man. For example, poly(I,C) is able to reduce the severity of experimentally produced rhinovirus infections when given intranasally but because of its inherent toxic properties, clinicians are proceeding cautiously in advocating its use as part of the antiviral armamentarium.

3.5. Miscellaneous Antiviral Agents

3.5.1. Thiosemicarbazones

The initial discovery that thiosemicarbazones possessed antiviral activity was made by *Hamre*[88-90] who observed a dramatic effect on mortality when benzaldehyde thiosemicarbazone *(13a)*, the *p*-acetamide homolog *(13b)*, and their *N*-isobutyl homologs *(13c)* and *(13d)* were administered to mice innoculated intranasally with vaccinia virus.



(13)

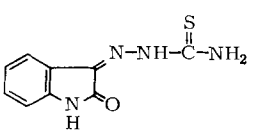
(13a), X = H, R = H

(13b), X = *p*-CH_3–C(=O)–NH, R = H

(13c), X = H, R = $CH(CH_3)C_2H_5$

(13d), X = *p*-CH_3–C(=O)–NH, R = $CH(CH_3)C_2H_5$

This development ultimately led to a study of other thiosemicarbazones by *Thompson et al.*[91] who observed a positive effect against this virus with isatin β-thiosemicarbazone *(14)*, when administered in a diet containing 0.6% of the drug.



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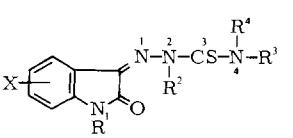


(15)

A further study of the efficacy of this compound by *Bauer*[92] indicated that mice medicated subcutaneously with two daily doses of 125 mg/kg each exhibited an excellent survival rate. A structure-activity study was next undertaken by *Bauer*[93] to determine the effects on antiviral activity of the modification of various portions of the isatin β-thiosemicarbazone structure *(15)*. *Bauer* concluded that introduction of substituents into the aromatic ring resulted in reduction or loss of activity. Substitution on the ring nitrogen (R') produced a sharp rise in activity reaching a peak with R'=ethyl. Substitution on the 2 or 4 position of the semicarbazone moiety resulted in complete loss of activity.

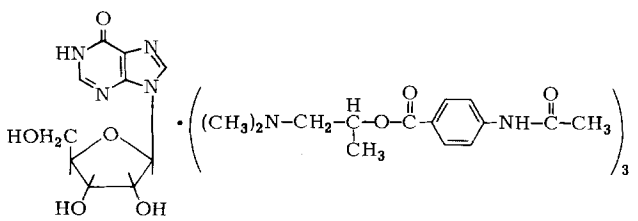
N-Methylisatin β-thiosemicarbazone (methisazone) *(15)*, R'=CH_3, R=H, was selected for further *in vivo* studies and was found effective against both DNA and some RNA viruses[94]. Clinically, the use of the drug has been confined to DNA viruses where it has shown a prophylactic effect

against smallpox[95]. If the disease is clinically apparent the drug is not effective; however, when administered during the incubation period, it diminishes the chance of developing the disease. Thus, in unprotected contacts, vaccination is indicated prior to the treatment with methisazone. Therapeutically, methisazone is effective in complications of vaccination such as viremia vaccination and vaccinia gangrenosa.

3.5.2. Immunostimulators

Although vaccines may be properly classed as immunostimulators, their activity is limited to antibody response to a specific organism as illustrated by smallpox, rubella, and other vaccines. Of late, studies have uncovered the ability of certain compounds to mobilize the body's total resistance mechanism and produce a higher level of resistance in response to an antigen than one would normally expect.

Inosiplex (isoprinosine) *(16)*, was found to be an immunostimulator and in the past several years has been evaluted as an antiviral agent.

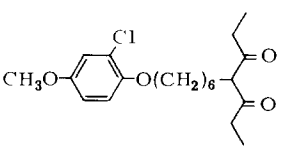


(16)

Thus far, the compound has not been significantly effective against influenza-A in mice[96]. A study in volunteers challenged with A2/Hong Kong influenza virus indicated no effect on the clinical symptoms but did produce a decrease in the amount of virus shed[97]. The administration of Inosiplex orally (1.5 mg qid for 9 days) caused a decrease in the incidence and severity of the illness with a concomitant increase in antibody titers[98]. Inosiplex has been found effective orally against herpes progenitalis, but it was unable to prevent the occurrence of relapse[99].

3.5.3. β-Diketones

Recently, *Diana* and *Pancic* have reported on the antiviral activity of a series of β-diketones[100]. One compound, 4-[6-(2-chloro-4-methoxyphenoxy)hexyl]-3,5-heptanedione *(17)* was



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selected for extensive evaluation *in vitro* and was found effective against rhino- and herpesvirus types 1 and 2. The efficacy against herpesvirus was confirmed in animal models and clinical studies are planned.

4. Conclusions

The most notable advance in the past decade in the area of antiviral chemotherapy has been the development of drugs which are currently in limited clinical use. More is known concerning the structure of viruses and viral replication, making it possible to design compounds which might interfere with viral processes. The stigma attached to antiviral compounds as necessarily being toxic to mammalian cells may become as antiquated as is the assumption that any potential major antiviral agent must be a nucleoside.

It has been stated many times that the advances in antiviral chemotherapy can not be considered analogous to those of antimicrobial chemotherapy. Among the factors which differ between the two are the nature of the resulting diseases, the structure of the organism, and the breadth of the spectrum of activity of the currently available antiviral agents *versus* that of the antibiotics.

Although some experimental drugs are active orally, more success is being achieved with local application, even to the extent of experimentally administering drugs intranasally for upper respiratory infections. This type of therapy could, in fact, have the advantage of reducing drug-related toxicity.

A major factor contributing to the rapid progress in the area is the development of more sophisticated and realistic *in vivo* models. Hopefully, these new models will lead to new, and more effective drugs.

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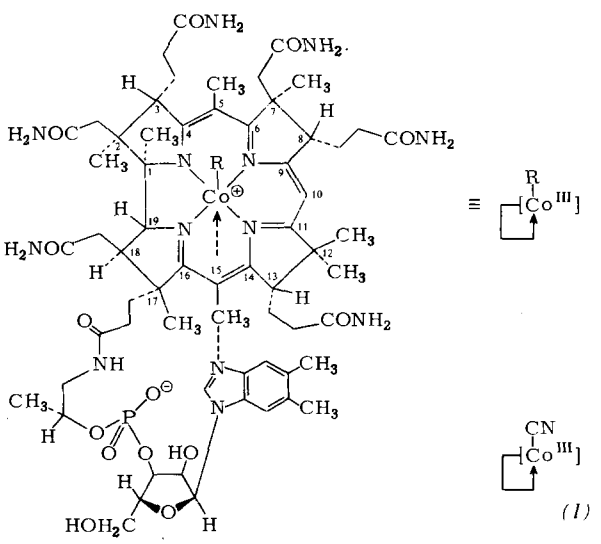
New Developments in the Field of Vitamin B_{12}: Reactions of the Cobalt Atom in Corrins and in Vitamin B_{12} Model Compounds

By G. N. Schrauzer[*]

Studies with vitamin B_{12} model compounds such as the cobaloximes provide a basis for the understanding of the mode of action of corrinoid coenzymes in enzymatic reactions. They also widen our knowledge of the properties and reactions of organocobalt compounds. The present article outlines the most important nonenzymatic reactions of cobalt in vitamin B_{12} and in model compounds of the cobaloxime type.

1. Introduction

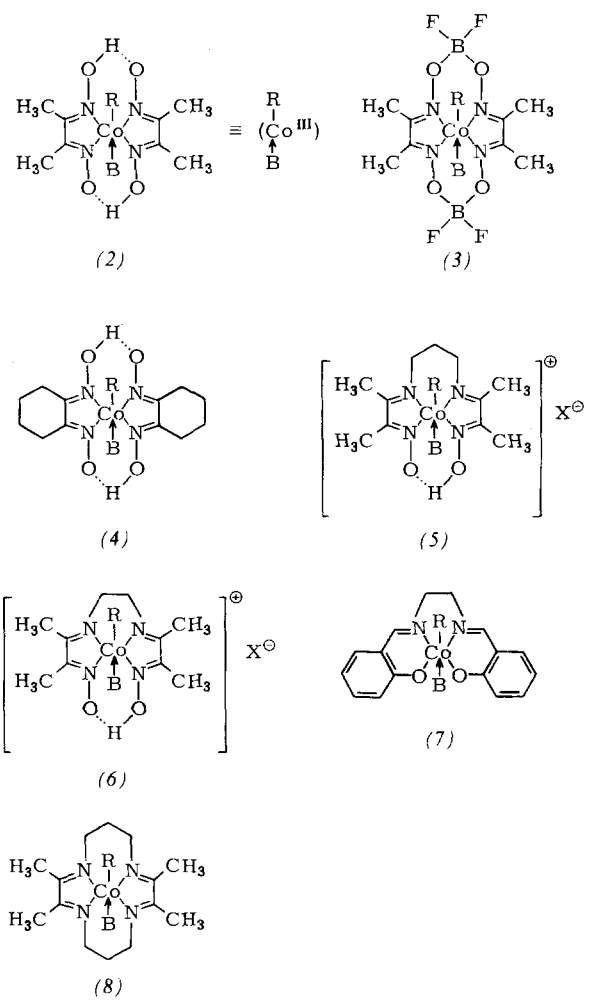
The last extensive report on chemical and biochemical developments in the field of vitamin B_{12} (cyanocobalamin) was published in this Journal in 1964[1], shortly after *Crowfoot-Hodgkin* and *Lenhert* demonstrated that coenzyme B_{12} (5'-deoxy-5'-adenosylcobalamin) contains a direct cobalt-carbon bond[2]. This important result indicated for the first time that organometallic reactions occur in biological systems. In view of the complicated structure of vitamin B_{12} *(1)* (see Scheme 1) it furthermore appeared reasonable to assume that the macrocyclic ligand system modifies the properties of cobalt significantly, enabling it to form stable Co—C bonds, for at that time only few rather unstable compounds were known to have Co—C-σ bonds.



(1)

Scheme 1. Structure of an organocobalamin. In vitamin B_{12} (cyanocobalamin) *(1)* R=CN; in coenzyme B_{12} R=5'-deoxy-5'-adenosyl. The ligand system having carbon atoms 1 to 19 and the four central nitrogen atoms is called corrin; see *(9)* in Section 4.

In 1964 *Schrauzer* and *Kohnle*[3] reported that the reactions of the cobalt atom in vitamin B_{12} can be simulated with much simpler complexes. The cobalt(III) complexes of diacetyldioxime *(2)*[4], which were first prepared by *Tschugaev* in 1907, resemble vitamin B_{12} so closely in their chemical properties that they were introduced as coordination-chemical models of vitamin B_{12}, and were named the "cobaloximes" to stress their similarity to the cobalamins. In the ensuing years numerous papers appeared in the literature[4] which confirmed the validity of cobaloximes as vitamin B_{12} model compounds. Other cobalt chelates were studied (see, *e.g.* [4, 5]) and proposed as alternative models (Scheme 2), but it eventually became clear that the simple cobaloximes of type *(2)* simulate the reactions of vitamin B_{12} most closely, both qualitatively and quantitatively. Since they are easily prepared and the required reagents can be found in every inorganic laboratory, none of the other cobalt chelates studied to date have challenged



(2) *(3)* *(4)* *(5)* *(6)* *(7)* *(8)*

Scheme 2. Structures of cobaloxime *(2)* and of other vitamin B_{12} model compounds *(3)* to *(8)*. In a wider sense, cobaloximes can also contain H, alkyl, or aryl [in place of CH_3 as in *(2)*]. B=base; R=CN, CH_3, C_2H_5, C_6H_5, *etc.*

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the leading position of the cobaloximes in the field of vitamin B_{12} model chemistry. Even ten years ago it was reasonable to expect that studies with cobaloximes would play a role in the eventual elucidation of the mechanism of action of vitamin B_{12}- or coenzyme B_{12}-catalyzed enzymatic reactions[6]. There can be no doubt that this expectation has been fulfilled, even though more work remains to be done. This report outlines the most important properties and reactions of the cobalt atom in the cobalamins as well as in the cobaloximes. Current theories and hypotheses concerning biochemical mechanisms of reactions involving vitamin B_{12}-coenzymes will be discussed in a future paper.

2. Nomenclature

Extensive guidelines for the nomenclature of vitamin B_{12} derivatives exist which will not be described here (for details see, *e.g.*,[7]). The cobalamins (more precisely: cob(III)alamins) contain 5,6-dimethylbenzimidazole as an additional axial ligand, which is linked to the corrin system through a ribofuranosyl-phosphate chain (see Scheme 1). In the cobamides the axial ligand is missing, but the ribofuranosyl-phosphate moiety is still present. The latter may be removed by acid hydrolysis, yielding cobinamides. For our present purposes it is usually not necessary to distinguish cobalamins from cobamides or cobinamides, all will be simply represented by [Co]. The reduced forms of vitamin B_{12} are known as vitamin B_{12r} (cob(II)alamin) and vitamin B_{12s} (cob(I)alamin). The former is a derivative of divalent cobalt, the latter of monovalent cobalt. In cyanocobalamin (vitamin B_{12}) and hydroxocobalamin (vitamin B_{12a}), cobalt is trivalent [see eq. (a)]. We shall represent cobaloximes, which also contain trivalent cobalt, simply by (Co), reduced derivatives will be designated cobaloxime(II) or cobaloxime(I) [see eq. (b)]. All other modifications of the abbreviated nomenclature are obvious. The axial bases in cobaloxime complexes will often not be identified as such and simply represented by "B" (see Table 1).

Table 1. Survey of nomenclature of cobalamins and cobaloximes.

Name	Cobalamines	Cobamides	Cobinamides	Cobaloximes
Constituents	Cobalt(III) + Subst. corrin + Ribofuranosyl phosphate + 5,6-Dimethylbenzimidazole + R	Cobalt(III) + Subst. corrin + Ribofuranosyl phosphate	Cobalt(III) + Subst. corrin	Cobalt(III) + Subst. bis-(glyoxaldioxime) + Base + R
Abbreviations used				
	or	[Co^{III}] or [Co]	[Co^{III}] or [Co]	or
Modifications				
		[Co^{II}]	[Co^{II}]	(Co^{II})
		[Co^{I}]$^{\ominus}$	[Co^{I}]$^{\ominus}$	(Co^{I})$^{\ominus}$

3. Structure

The structure of the first organocobaloxime was determined by *Lenhert*[8] in 1967 and is shown in Figure 1. The observed in-plane Co—N bond distances are essentially identical to those observed in coenzyme B_{12}. The Co—C bond length is also

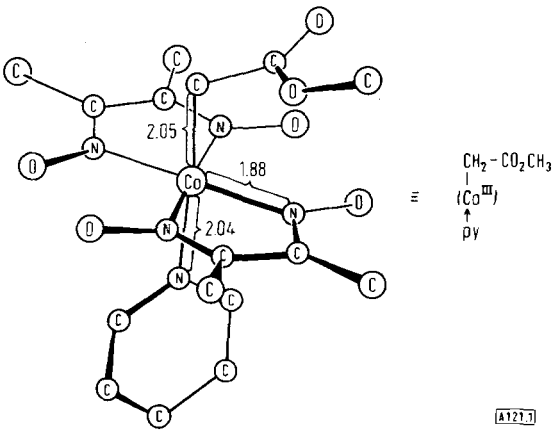
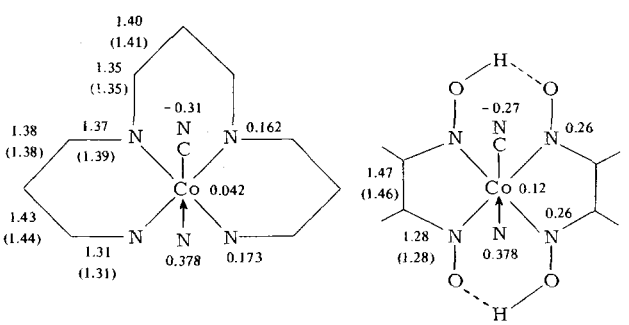


Fig. 1. Structure of methoxycarbonylmethyl(pyridine)cobaloxime (according to [8], distances in Å). Hydrogen atoms are not shown.

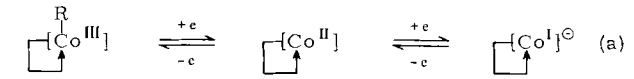
virtually the same, but the axial Co—N distance is somewhat shorter in the cobaloxime than in the cobalamin. We concluded from this that the cobalt in the cobaloximes might carry a slightly greater partial positive charge than in the cobalamins; this suggestion was substantiated by LCAO-MO calculations (see Scheme 3).



Scheme 3. Calculated (experimental) bond distances and π-electron charge distribution in the ground state of models of cyanocobalamin (left) and of the corresponding cobaloxime derivative (right) [16].

4. General Considerations

The biological activity of vitamin B_{12} coenzymes must undoubtedly be associated with the presence of cobalt, whose oxidation-reduction potentials are modified by incorporation into the corrin system. It can now exist not only as a di- and trivalent, but also as a monovalent entity [eq. (a)][11].

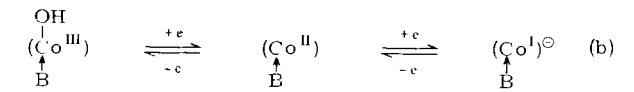


Hydroxo-cobalamin
Vitamin B_{12a}
purple

Vitamin B_{12r}
brown

Vitamin B_{12s}
blue-green

The cobaloximes behave analogously [eq. (b)][9, 10]

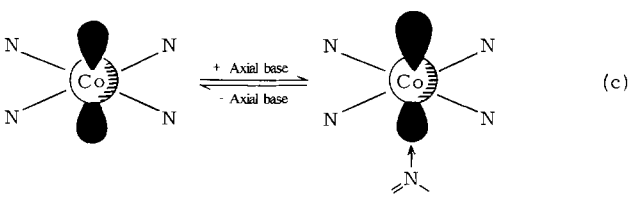


Hydroxo-cobaloxime
red-brown

Cobaloxime (II)
brown

Cobaloxime (I)
blue or blue-green

In the cobalt(I) derivatives, the metal is in a spin-paired d^8 configuration. Two electrons occupy the weakly antibonding $3d_{z^2}$ orbital, and the resulting electron distribution is responsible for the high nucleophilic reactivity of cobalt(I)[11, 12]. Cobalt(I) in the cobaloximes interacts with bases, giving rise to changes in the optical absorption spectrum and chemical reactivity. There is evidence that one molecule of the base interacts with cobalt(I) in the axial position. This changes the electron-distribution of the d_{z^2} orbital as shown in eq. (c). "Hard" bases such as OH^- increase the electron density on cobalt, unsaturated nitrogen bases lower the elec-



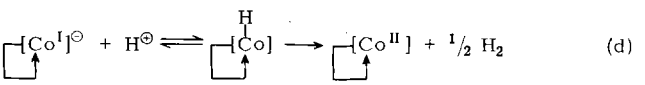
(c)

tron density through d_π-p_π interactions. The latter effect leads to a slight diminution of the nucleophilic reactivity. The position of vitamin B_{12s} and of cobalt(I) derivatives of model compounds in *Pearson*'s Nucleophilicity Scale[13] is shown in Table 2. It may be seen that the cobalt(I) derivatives are some of the most powerful nucleophiles known and for this reason have been called "supernucleophiles". Although certain cobalt(I) complexes are apparently even more nucleophilic than vitamin B_{12s} (cob(I)alamin), the latter is presumably the most powerful nucleophile of Nature, especially since it can be readily generated in the physiological pH range. The cobalt(I)-porphyrins, on the other hand, are capable of existence only in nonaqueous media, *e.g.* pyridine, and decompose in water spontaneously with evolution of hydrogen. Vitamin B_{12s} and cobaloximes(I) decompose in neutral or weakly alkaline solutions (pH 10) as well [(eq. (d)], but the rates are comparatively slow.

Table 2. Pearson nucleophilicities [13] (based on CH_3I) of a number of cobalt(I) derivatives and other nucleophiles.

Nucleophile [a]	$n_{Pearson}$
CH_3OH	0.00
Cl^-	4.37
NH_3	5.50
Br^-	5.79
I^-	7.42
CN^-	6.70
$C_6H_5S^-$	9.92
$S_2O_3^{2-}$	6.90
$P(C_6H_5)_3$	8.69
$C_6H_5Se^-$	*ca.* 10.7
$(C_6H_5)_3Sn^-$	*ca.* 11.5
Rhodoxime(I) [H_2O or OH^-]	13.7
Cobaloxime(I) [Pyridine]	13.8
Cobaloxime(I) [H_2O or OH^-]	14.3
Cobinamide(I) [H_2O or OH^-]	14.4
Vitamin B_{12s}	14.4
Cobalt(I)-Salen [b]	*ca.* 14.6
Cobalt(I)-Porphyrins	*ca.* 14.6

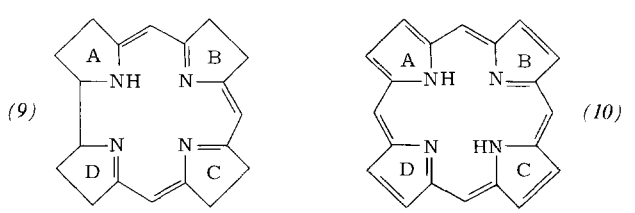
[a] Axial base components in square brackets.
[b] Salen is the tetradentate ligand in *(7)*.



Hydridocobalamin

The decomposition according to eq. (d) is accelerated by noble metal catalysts, *e.g.* Pt; vitamin B_{12s} is a metastable compound in the physiological pH range. The corresponding Brønsted acid hydridocobalamin is unstable in aqueous media. It is presumably a weak acid, since the corresponding hydridocobaloximes are also only weakly dissociated. Solutions of hydridocobalamin are obtained if vitamin B_{12a} (hydroxocob(III)alamin) is reduced with zinc in glacial acetic acid. Generated under these conditions, hydridocobalamin has sufficient life-time to be characterized by its reactions with a variety of substrates and its absorption spectrum. Its reactivity differs from that of vitamin B_{12s}, as will be outlined below (see Section 7).

Cobalt-porphyrins do not occur in Nature, or at least have never been isolated. We would not expect them to have any physiological activity if only because they cannot be reduced to, or maintained in, the Co^I state in aqueous solution. This fact may be used to explain some of the most striking differences between the structure of the corrin system *(9)* and that of the porphyrins *(10)*. Both are related biogenetically, but in *(9)* rings A and D are connected through a direct C—C bond. This causes a marked distortion of the coordination symmetry of the ligand and produces and odd-numbered π-electron system which exists only as a monoanion. The porphyrin ligand possesses an even number of constituent atoms, is highly symmetrical and in metal complexes is present as the dianion. These structural differences cause a weakening of the effective coordinating power of *(9)* relative to *(10)*, which in turn lowers the Co^{II}/Co^I reduction potential.



(9) *(10)*

The azomethine system in *(9)* is reasonably resistant to reducing agents and can be hydrogenated to colorless deriva-

tives only under relatively drastic conditions. The peripheral substituents protect the vitamin B_{12} chromophore against dehydrogenating attack. The propionamide side-chains endow the molecule with hydrophilic character, but the various substituents also serve as points of attachment of the vitamin to apoenzymes or transport proteins.

If it is assumed that vitamin B_{12} functions biologically at least in some cases as a nucleophile, it can be rationalized why the central metal must be cobalt. Of all other elements, only the rare element rhodium could replace cobalt in some of its functions. Rhodium analogs of vitamin B_{12}, *e.g.* a (5,6-dimethylbenzimidazolyl)rhodibamide, have recently become known[14], but initial tests indicate biological inactivity. Investigating the reactions of "rhodoximes", *i.e.* the Rh analogs of the cobaloximes, we predicted[15] that Rh-B_{12} derivatives should be either biologically inactive or less active than vitamin B_{12}, since rhodium(I) nucleophiles are not as reactive as the corresponding cobalt(I) derivatives. Organometallic derivatives of rhodoximes furthermore are as a rule more stable or chemically resistant than organocobaloximes, the same should be true for the respective rhodibamides relative to cobamides.

Why is the 6th coordination position of cobalt blocked with a base, such as 5,6-dimethylbenzimidazole? An at least partial answer to this question can be given if one considers that the Co—C bond in organocorrins is susceptible to reductive cleavage through axial attack. The axial base thus functions as a protecting group and assures that cobalt-bound organic substituents such as the 5′-deoxyadenosyl residue of the coenzyme is not lost due to nonspecific interactions with biogenic reductants.

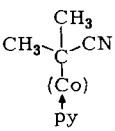
5. Electronic Structure and Bonding

The striking analogies between the chemical properties of the cobalt atom in vitamin B_{12} and in the cobaloximes are primarily a consequence of a fortuitous identity of the effective coordinating power of the four sp^2-hybridized nitrogen atoms in the otherwise unrelated ligand systems. LCAO-MO-calculations (Scheme 3)[16] confirmed this conclusion, since they revealed a nearly identical charge distribution in the atoms surrounding the cobalt atom. The eigenvalues and -vectors of the axial cobalt-ligand bonds were also found to be essentially the same. However, the calculations revealed that the partial positive charge on cobalt is somewhat higher in the cobaloximes than in vitamin B_{12}. This causes a firmer attachment of axial bases in the model compounds as compared to corrins and introduces some differences in reactivity. However, the overall orbital-stabilizing effects of the corrin ligand are by no means specifically dependent on details of the electronic structure of the azomethine system in the molecule, thus permitting their simulation with unrelated simpler ligands. Nevertheless, the original selection of biacetyldioxime complexes *(2)* of cobalt(III) as vitamin B_{12} models was in part fortunate, since the properties of the cobalt complexes depend on the nature of the peripheral dioxime substituents as well. For example, bis(benzildioximato)cobalt complexes are already less suitable for model work, if only because their Co(I) derivatives are less nucleophilic than vitamin B_{12s} or bis(biacetyldioximato)cobalt(I).

The systematic study of other cobalt chelates did not provide any better models of vitamin B_{12}, but furnished examples of nucleophiles with $n_{Pearson}$ values ranging between 10 and 15, *i.e.* supernucleophiles. Substitution of the oxime protons by BF_2 groups yielded complexes of type *(3)* which also proved to be much less nucleophilic than the parent cobaloxime(I) species. A number of Schiff base complexes of cobalt proved somewhat more nucleophilic, but offered no advantage over the cobaloximes. The chelates *(5)* and *(8)* were found to form dialkylcobalt derivatives[17, 18], in contrast to the behavior of cobaloximes, and thus can no longer be regarded as *bona fide* models of vitamin B_{12}. Pentacyanocobalt complexes are known to form organometallic derivatives and have therefore been temporarily regarded as vitamin B_{12} models[19].

6. Reactions of Cobalt(I) Supernucleophiles

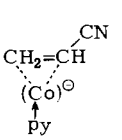
The cobalt(I) supernucleophiles react with conventional alkylating agents to yield organocobalt complexes, the reactions are nucleophilic substitutions and occur with inversion at the α-carbon atom[20]. Epoxides and certain cyclopropane derivatives also react with the cobalt(I) chelates. Stable organocobalt compounds are as a rule formed only if the cobalt-bound carbon is primary or secondary[21]. Tertiary derivatives are isolable only in rare instances. The cobaloxime *(11)* is sufficiently stable to be isolated, but the corresponding derivative of vitamin B_{12} cannot be obtained. This suggests steric hindrance by the corrin ligand. However, electronic effects influence the stabilities of the organocobalt complexes as well.

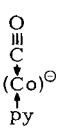


(11)

The cobalt(I) derivatives of cobaloximes form π complexes with activated olefins, for example, with acrylonitrile *(12)*; they also form adducts with carbon monoxide *(13)*. There is some evidence that vitamin B_{12s} also forms π complexes with activated olefins, but these appear to be less stable than the corresponding complexes with cobaloximes (I)[22].

(12)



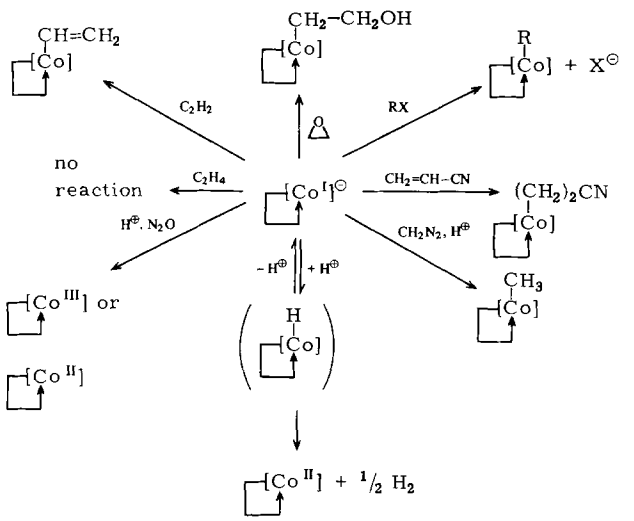


(13)

The π-complex bound axial ligands effectively block the cobalt(I) ion against nucleophilic attack by alkylating agents, although the complexes are labile, and the π-bound ligands can be readily removed, *i.e.* by passing argon through the solutions. The free cobalt(I) nucleophiles are all extremely oxygen-sensitive. They are also oxidized by N_2O[23]. The reaction with N_2O is of interest as it occurs only with cobalt(I), and not with cobalt(II) derivatives. The specific oxidizing action of N_2O was used as a means to detect the corrin nucleophile in certain enzymes, as will be outlined in a future paper. Typical reactions of vitamin B_{12s} (cob(I)alamin) are shown in Scheme 4.

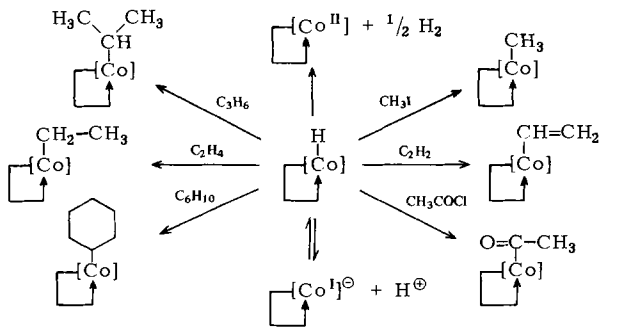
7. Hydridocobalamin and Hydridocobaloximes

It has already been mentioned in Section 4 that the Brønsted acid of vitamin B_{12s} (hydridocobalamin) is unstable in aqueous solution (Scheme 4). Most "hydridocobaloximes" are also unstable in water, especially if nitrogen bases occupy the 6th coordination position. With phosphanes as axial ligands, isolable hydridocobaloximes are formed[24]. Hydridocobaloximes are weak acids with pK_a-values in the order of 10^{-10}. Hydrido(tributylphosphane)cobaloxime is dark blue and is surprisingly soluble in nonpolar media, including *n*-hexane. The hydride is relatively unreactive in nonpolar aprotic solution. For example, no reaction occurs with methyl iodide, ethylene oxide, or ethyl acrylate in dry *n*-hexane.



Scheme 4. Some reactions of the vitamin B_{12} cobalt(I) supernucleophile (vitamin B_{12s}, cob(I)alamin). Cobaloximes(I) also undergo these reactions.

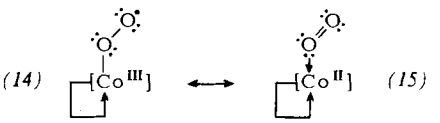
The reduction of hydroxocobalamin (vitamin B_{12a}) with zinc in glacial acetic acid affords solutions of hydridocobalamin[25]. Hydridocobalamin differs from vitamin B_{12s} in that it reacts with simple nonactivated olefins to yield alkycobalamins. With ethylene, ethylcobalamin is formed; with propylene, isopropylcobalamin. Cycloolefins such as norbornene, cyclooctene, and even cyclododecatriene react with hydridocorrins as well to yield secondary cycloalkyl cobalt derivatives which were previously not readily accessible. Some of the reactions of hydridocobalamin are summarized in Scheme 5. Further studies with this interesting compound are presently still in progress.



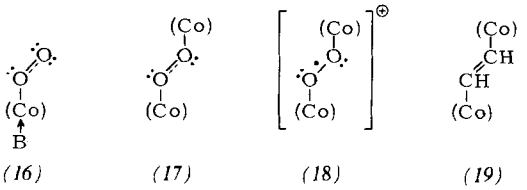
Scheme 5. Some reactions of hydridocobalamin (generated from vitamin B_{12a} by reduction with zinc in glacial acetic acid).

8. Electronic Structure and Reactivity of Cobalt(II) Derivatives

In vitamin B_{12r} and the cobalt(II) derivatives of the cobaloximes the cobalt ion is in a d^7 configuration, the unpaired electron occupies the $3d_{z^2}$ orbital. EPR measurements show that the axial ligand 5,6-dimethylbenzimidazole in vitamin B_{12r} is attached to cobalt[26,27]. Cobaloximes(II) form 1:1 and 1:2 adducts with a variety of bases[28]. The 1:1 adducts are diamagnetic in the solid state, therefore suggesting a dimeric structure with a Co—Co bond. A dimeric rhodoxime with a Rh—Rh bond is known[29]. Vitamin B_{12r} shows no tendency to dimerize, presumably for steric reasons, it also does not generally form adducts with two molecules of base. Vitamin B_{12r} and cobaloximes(II) react with oxygen to yield peroxo complexes. Peroxocobalamin[30] may be regarded as a charge-transfer type complex. Two limiting structures can be written, of which *(14)* has the greatest weight, as evidenced by EPR analysis. Vitamin B_{12r} is a nearly reversible oxygen carrier.



Cobaloximes(II) react with oxygen to yield three different compounds *(16)*—*(18)*. Peroxocobaloximes *(16)* in solution show EPR spectra which are virtually identical to those of peroxocorrins. However, cobaloximes(II) also form diamagnetic μ-peroxodimers of type *(17)*. The latter tend to convert into μ-peroxoradicals *(18)*, presumably by way of a disproportionation reaction. Cobaloximes(II) react with acetylene as well to yield the compound *(19)*[21]. They also react with alkylating agents under certain conditions[21]. On reaction with benzyl halides, benzylcobaloximes are formed[31], the reaction is assumed to be of a free-radical type. It is possible that the reaction of cobaloximes(II) with CCl_4 [eq. (e)][32] also involves homolytic C—Cl bond cleavage.



$$CCl_4 + 2\ (Co^{II}) \longrightarrow \underset{(Co)}{\overset{CCl_3}{|}} + \underset{(Co)}{\overset{Cl}{|}} \qquad (e)$$

Methyl radicals, generated in solution, have been shown to react with vitamin B_{12r} to yield methylcobalamin. Cobaloximes(II) act as catalysts in the reduction of cobaloximes(III) by carbon monoxide [eq. (f)[33]]. The reduction of hydroxocobalamin by carbon monoxide in aqueous solution is also catalyzed by vitamin B_{12r}[34].

Cobaloximes(II) disproportionate in alkaline solution to yield cobalt(III) and cobalt(I) derivatives; the corresponding reaction of vitamin B_{12r} occurs more slowly. Cobaloximes(II),

$$\overset{X}{\underset{|}{(Co^{III})}} + CO + 2\ OH^{\ominus} \xrightarrow[(Co^{II})]{} (Co^{I})^{\ominus} + CO_2 + H_2O + X^{\ominus} \quad (f)$$

but not vitamin B_{12r}, react with molecular hydrogen. The reduction of cobaloximes(III) by H_2 is catalyzed by cobaloximes(II) and yields the cobalt(I) nucleophiles [eq. (g)][21].

$$\overset{X}{\underset{|}{(Co^{III})}} + H_2 + 2\ OH^{\ominus} \xrightarrow[(Co^{II})]{} (Co^{I})^{\ominus} + 2\ H_2O + X^{\ominus} \quad (g)$$

Reaction according to eq. (g) proceeds readily even below room temperature at 1 atm of H_2 and in neutral or alkaline buffered aqueous media. This method of generating the cobalt(I) nucleophiles or hydridocobaloximes is useful for the synthesis of organocobalt complexes. Reacting cobaloximes(II) with H_2 in alkaline solutions yields the cobalt(I) nucleophiles, which react with *e.g.* acrylates to yield β-alkoxycarbonylethylcobaloximes. In neutral buffered solutions hydridocobaloximes are formed as such or *in-situ*; their reaction with acrylic esters affords the corresponding α-isomers[24].

$$(Co^{II}) + {}^1/_2\ H_2 \xrightarrow[\text{pH 10-11}]{} (Co^{I})^{\ominus} \quad (h)$$

$$\xrightarrow{+\ CH_2{=}CH{-}COOR + H^{\oplus}} \underset{(Co)}{CH_2{-}CH_2{-}COOR}$$

$$(Co^{II}) + {}^1/_2\ H_2 \xrightarrow[\text{pH 7-8}]{} \underset{(Co)}{H} \quad (i)$$

$$\xrightarrow{+\ CH_2{=}CH{-}COOR} \underset{(Co)}{H_3C{-}CH(COOR)}$$

With monosubstituted alkynes α- or β-substituted vinylcobaloximes are formed in analogy to eq. (h).

The reaction of cobaloximes(II) with H_2 in the presence of primary amines and formaldehyde gives rise to the formation of *N*-methylated amines *via* isolable aminomethylenecobaloximes *(20)* [eq. (j)][35].

$$CH_2{=}O + RNH_2 + (Co^{II}) + {}^1/_2\ H_2 \xrightarrow[-H_2O]{} \underset{(Co)}{CH_2{-}NHR} \quad (20) \quad (j)$$

$$\xrightarrow{+H_2} CH_3NHR + (Co^{I})^{\ominus} + H^{\oplus}$$

This reactions shows some analogy to *Wallach*'s aminomethylation method and can also be performed catalytically. With thiols in place of amines, the corresponding methylthio compounds are obtained, but in this case intermediate organocobaloximes analogous to *(20)* could not be isolated. A complex of type *(20)*, with $R = C_6H_5$, reacts with NO_2^- to yield a compound in which the $-CH_2-N(NO)-C_6H_5$ residue is attached to cobalt. The reductive cleavage of the Co—C bond in such complexes affords the carcinogenic *N*-methyl-*N*-nitrosoaniline[36].

9. Reactions of the Cobalt(III) Derivatives

The first organocobalt derivatives of corrins[1] and of cobaloximes[3] were synthesized by the reaction of the corresponding Co^{III} derivatives with organomagnesium halides. In aqueous solution, organocobalt complexes can be obtained from Co^{III} derivatives on reaction with carbanions, eq. (k) may be cited as an as yet unpublished example:

$$\overset{OH}{\underset{|}{(Co^{III})}} + [NC{-}\ddot{C}H{-}COOC_2H_5]^{\ominus} \longrightarrow \quad (k)$$

$$\underset{(Co)}{NC{-}CH(COOC_2H_5)} + OH^{\ominus}$$

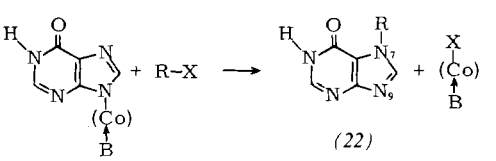
Vinyl ethers react with cobaloximes(III) as well as with hydroxocobalamin in the presence of bases to yield derivatives of formylmethylcobaloxime and -cobalamin, respectively [eq. (l)][37].

$$CH_2{=}CH{-}OR \xrightarrow{+\ OR^{\ominus}} \ddot{C}H_2{-}CH(OR)_2 \xrightarrow{+\ (Co^{III})} \underset{(Co)}{CH_2{-}CH(OR)_2} \quad (l)$$

(21)

The acetals *(21)* can be saponified to the corresponding formylmethylcobalt complexes under appropriate conditions. It is of interest that the acid-cleavage of diacetals and of hemiacetals of formylmethylcobalamin occurs with extensive Co—C bond cleavage. Formylmethylcobalamin was also prepared by the reaction of vitamin B_{12s} (cob(I)alamin) with bromoacetaldehyde. This compound is stable in neutral aqueous solution just as the corresponding cobaloxime derivative, both decompose in acidic media to yield acetaldehyde[38, 39].

Ligand-exchange reactions of cobaloximes(III) have been extensively investigated by many workers and will not be discussed in any detail[40]. A cobaloxime(III) was recently employed for the stereospecific synthesis of N^7-alkylated xanthine and hypoxanthine derivatives. The purine bases are first attached to the Co of the cobaloxime, affording N^9-coordinated adducts whose subsequent alkylation produces the N^7 substituted alkyl purines *(22)* as exemplified in eq. (m)[41].



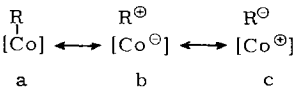
(22) (m)

It may be expected that cobaloximes will become useful reagents in synthetic organic chemistry. Recently, cobaloximes were employed as protecting groups in the synthesis of certain amino acid derivatives[42].

10. Properties and Reactions of the Organocobalt Compounds

Although organocobalt complexes of vitamin B_{12} and of model compounds are routinely described as cobalt(III) com-

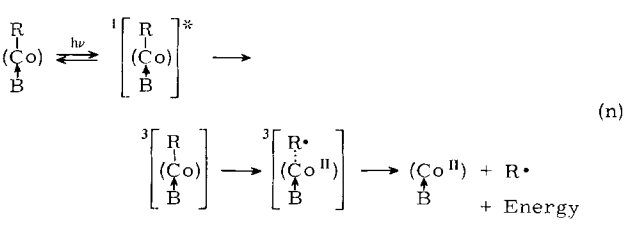
plexes, this formalism can lead to misunderstandings as it ignores the high covalency of the Co—C bonds. It is more realistic to describe the nature of the axial Co—C bonds in terms of the limiting structures a to c; structure a is the most important:



LCAO-MO calculations indicate that the interactions of the carbon sp^3 orbital with the $3d_{z^2}$, $4p_z$, and 4s orbitals of cobalt are mainly responsible for bond stabilization. The axial bonds in cobaloximes and cobalamins possess very similar energy and can be described as multicenter bonds[16]. The organic residue R is accordingly influenced through cobalt by the axial base B, and *vice versa*. These *trans* effects, or vertical conjugation effects, have indeed been detected experimentally. If the organic residue R is an sp^2- or sp-hybridized carbon atom, additional interactions of the π-carbon orbitals with the $3d_{xz}$ and $3d_{yz}$ orbitals of cobalt occur and lead to a stabilization of the axial bond. The axial bond MOs also interact to some extent with the orbitals of the horizontal ligand systems. The axial bonds thus are slightly delocalized over the whole molecule of the complex. The effects of the axial groups on the horizontal ligands are not very important chemically. They are, however, responsible for characteristic changes of the absorption spectra, particularly of vitamin B_{12} derivatives. The effects of variation of the axial substituents on the transition energies of cobalamins have been calculated and are in reasonable agreement with experimental data[7,43].

10.1. Photolysis and Thermolysis of Methylcobalt Complexes

In the absorption spectra of alkylcobaloximes, bands of weak to medium intensity are observed in the range between 350 and 470 nm ($\varepsilon = 1000$—3000). These have been assigned to transitions between axial bond MOs[16]. Irradiation of alkylcobaloximes with light of wavelengths between 500 and 350 nm causes an occupation of antibonding axial bond MOs, which induces the cleavage of the Co—C bond. During the excitation process, intermediate states of the complexes are generated which ultimately decompose into free radicals R• and cobaloxime(II) fragments [eq. (n)].



(n)

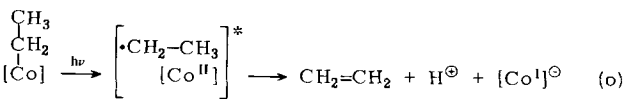
The subsequent reactions of the free radicals depend on their structure and reactivity. Methyl radicals recombine with the cobalt(II) fragments with high efficiency if the photolysis is performed under strictly anaerobic conditions in water. Accordingly, one finds that methylcobaloxime and methylcobalamin are rather resistant to photolysis under these conditions. Some of the methyl radicals diffuse out of the coordination sphere of cobalt and subsequently terminate either by dimerization to ethane, or by hydrogen abstraction, to methane. Photolysis of the same compounds in alcoholic solvents, particularly isopropanol, favors H-abstraction reactions and methane is formed virtually exclusively[44]. Some of the methyl radicals are reduced under the photolysis conditions. This explains, why CH_3D is formed in varying amounts if the methylcobalt complexes are photolyzed in D_2O as the solvent.

The photolysis of trideuteriomethyl-cobalamin and -cobaloxime, respectively, in H_2O produces ethane which consists to 89% of C_2D_6 and to 11% of CH_3CD_3. It appears that ligand-methyl groups are also cleaved off during the photolysis. If methylcobalt complexes are photolyzed in the presence of CN^- ions, methane becomes the main product. The axial coordination of cobalt by CN^- increases the electron density of cobalt; this apparently favors the reduction of methyl radicals. The aerobic photolysis of methyl cobalt complexes is complicated by radical-oxidation reactions. *Via* peroxide-type intermediates, formaldehyde is formed as one of the major products derived from the methyl radicals.

The methylcobalt complexes are stable thermally up to about 170 °C. They decompose at higher temperatures, during the decomposition methyl radicals are formed which terminate to yield methane and ethane as expected. This indicates that the Co—C bond undergoes homolytic cleavage during thermolysis. Photolysis of methylcobaloxime in the presence of vitamin B_{12r} gives rise to the formation of small amounts of methylcobalamin, the vitamin B_{12r} thus acts as a radical scavenger. Benzene similarly traps the methyl radicals produced on photolysis to yield toluene.

10.2. Photolysis and Thermolysis of Higher Alkylcobalt Complexes

During the photolysis of higher alkyl-cobaloximes or -cobalamins, radicals are also the primary products of Co—C bond cleavage. However, the subsequent reactions of the organic radicals are more complicated. Ethylcobalt complexes of vitamin B_{12} and of cobaloximes undergo photolysis to yield ethylene, the cobalt(II) fragments produced are reduced to cobalt(I) derivatives, which in turn decompose with release of hydrogen. The intermediate formation of the cobalt(I) species was clearly demonstrated[44–46]. The overall process can thus be expressed in terms of eq. (o).

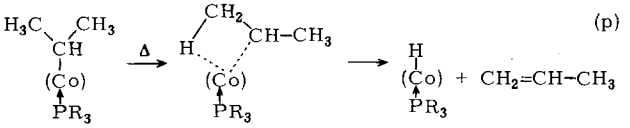


(o)

Higher alkylcobalt derivatives undergo photolysis in analogy to eq. (o), but if the reactions are carried out in alcoholic solvents instead of water alkanes are formed as well as olefins[44]. In the photolysis of alkylcobalt derivatives of salen *(7)*, alkanes are formed which arise from the dimerization of two alkyl radicals. This indicates that the behavior of alkyl radicals depends on the Co^{II}/Co^{I} reduction potential of the cobalt chelates.

Ethylene is the main product of the thermolysis of ethylcobalamin and -cobaloxime, respectively, but traces of ethane and of *n*-butane were also detected.

On aerobic photolysis of the higher alkylcobalt compounds aldehydes and other radical oxidation products are observed. Higher alkenylcobaloximes carrying a terminal C=C bond in the cobalt-bound organic residue produce alkenyl radicals on aerobic photolysis which undergo cyclization reactions prior to the termination step[47]. Alkylperoxo radicals which are formed during aerobic photolysis may also react with the cobaloxime(II) fragments to yield isolable alkylperoxocobalt complexes[47,48]. The quantum yields in typical photolysis reactions of alkylcobaloximes and -cobalamins have been determined[16,49]. Hydridocobaloximes are formed during the thermolysis of certain alkylcobaloximes. Isopropyl(tri-*n*-butylphosphane)cobaloxime decomposes on heating according to eq. (p), possibly *via* a cyclic transition state[24].

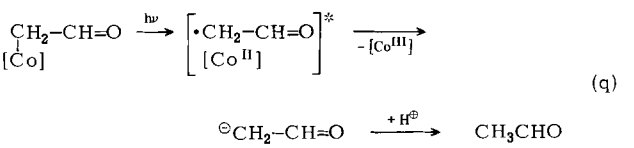


(p)

Another example of a hydridocobaloxime elimination reaction is described in ref. [50].

10.3. Photolysis and Thermolysis of Substituted Alkylcobalt Complexes

The behavior of substituted alkylcobalt complexes on photolysis and thermolysis is determined by the oxidation-reduction potential and constitution of the radicals which are formed during the initial process of Co—C bond cleavage. Inductively electron-attracting substituents in α-position give rise to radicals whose electron affinity may be sufficient to cause oxidation of the cobalt(II) fragments to the cobalt(III) species. The photolysis of formylmethylcobalamin is cited as a typical example [eq. (q)][38]. Acetaldehyde and hydroxocobalamin are the only detectable products, vitamin B_{12r} cannot be observed as it is apparently immediately oxidized to vitamin B_{12a}. Similarly, ethyl acetate is formed in the thermolysis of ethoxycarbonylmethylcobaloxime[21].



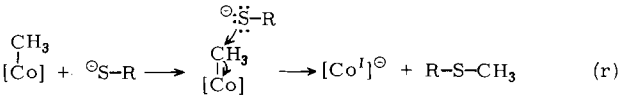
(q)

Substituents in the β-position relative to cobalt influence the photochemical behavior in several ways. Ethylene and acetaldehyde are produced during the photolysis of β-hydroxyethylcobaloxime, for example, indicating that both elimination and rearrangement reactions take place[51].

10.4. Chemical Cleavage of Cobalt-Carbon Bonds

The covalent Co—C bonds in the organocobalt complexes may be cleaved by nucleophilic as well as electrophilic attack, reductive cleavage reactions are also known. The reaction of *n*-alkylcobaloximes and -cobalamins with thiolate ions[52] have been studied in greater detail[53]. Kinetic measurements indicate that they proceed by an SN_2 mechanism [eq. (r)].

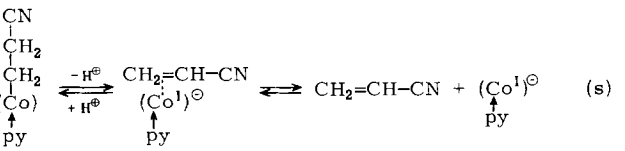
The methylcobaloxime derivatives also react with other nucleophiles, *e.g.* with Cl^-, Br^-, I^-, CN^-, $P(n\text{-}C_4H_9)_3$, $P(C_6H_5)_3$, $C_6H_5—NR^-$, Se^{2-}[54], and also with the cobalt(I) supernucleophiles themselves[54,55]. Higher alkylcobalt derivatives react with some of the nucleophiles as well, but frequently by way of β-elimination rather than nucleophilic substitution. Isopropyl(pyridine)cobaloxime reacts with tri-*n*-butylphosphane rapidly at 50 °C to yield propylene and hydri-



(r)

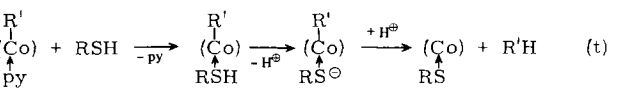
do(tri-*n*-butylphosphane)cobaloxime. Neopentyl(pyridine)cobaloxime, a compound which does not carry hydrogen in the β-position, does not undergo Co—C-bond cleavage, not even on heating with tributylphosphane to 100 °C; the only reaction which is observed is the displacement of the axially bound pyridine by the phosphane[54].

Electron-attracting substituents in the β-position increase the tendency of organocobalt complexes to undergo elimination reactions. β-Cyanoethylcobalamin[56] and the corresponding cobaloxime[21] are base-sensitive and decompose reversibly according to eq. (s)[22].



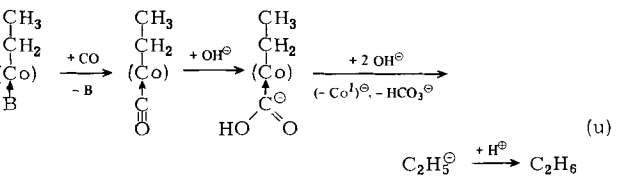
(s)

The reaction of organocobalt complexes with thiolate ions is strongly pH dependent. Nucleophilic transalkylation occurs in alkaline media at high RS^- concentrations. In neutral or weakly acidic solutions Co—C bonds are cleaved reductively according to eq. (t)[57].

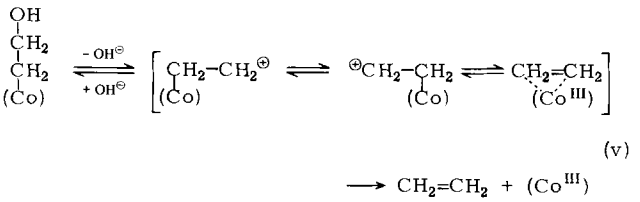


(t)

Reductive cleavage of Co—C bonds occurs preferentially with organocobalt complexes carrying electronegatively substituted alkyl residues. Reductive Co—C bond cleavage reactions were also observed with alkaline CO, stannite, and with dithionite[58]. The reaction with CO in alkali is exemplified for an ethylcobaloxime in eq. (u). The mechanism of Co—C bond cleavage by CO, particularly the *trans* attack in eq. (u), is supported by the observed formation of a CO adduct of methylcobaloxime in nonaqueous solvents[59].

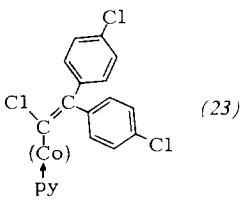


(u)



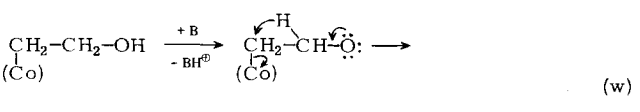
(v)

Cobaloximes and cobalamins with halogen in α-position of the cobalt-bound alkyl group have not yet been isolated. The reaction of cobaloximes(I) with 1,2-dichloroethane causes the spontaneous evolution of ethylene[61]; the presumed intermediate, 2-chloroethylcobaloxime, is evidently quite short lived. α-Haloalkylcobalt complexes are likewise sensitive to alkali. In the reaction of DDT with cobaloxime(I), a complex *(23)* is formed, indicating that not only substitution of Cl^- but also elimination of HCl took place[62,63].



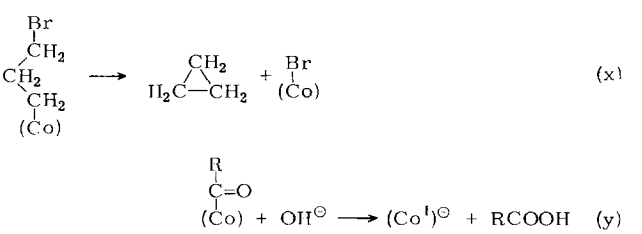
(23)

The base-induced cleavage of 2-hydroxyalkylcobalt complexes is of interest as it produces the cobalt(I) nucleophiles and aldehydes or ketones, respectively[51]. We assumed that reaction eq. (w) is a model of the enzymatic dehydration of ethylene glycol to acetaldehyde:



(w)

The substitution of hydrogen by halogen in γ-position affords stable organocobalt complexes. We found some time ago, however, that γ-bromopropylcobaloxime undergoes thermolysis with formation of cyclopropane [eq. (x)]. Acylcobalamins and -cobaloximes decompose in alkali according to eq. (y)[61,64].

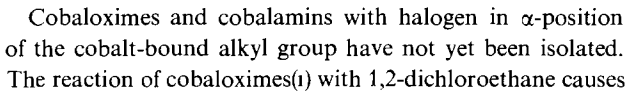


(x)

(y)

10.5. Reactions of Alkylcobalt Complexes with Metal Ions

Methylcobalamin, methylcobaloxime, and higher *n*-alkylcobalt derivatives of both, react with mercuric ion to yield alkylmercuric salts. The Co—C bond in methylcobalt complexes is cleaved by ions such as Au^{3+}, Tl^{3+}, Pt^{2+}, and Pd^{2+}, giving rise to methyl derivatives of metals which have been isolated in some cases[65,66]. The alkylcobalt derivatives of vitamin B_{12} and of cobaloximes thus behave in some respects just as typical organometallic compounds, although they should not be regarded as Nature's Grignard reagents. The cobalt-organic compounds are a rule much more resistant to solvolytic attack than simple organometallic compounds. To saponify *(24)* to the free acid *(25)* it is convenient to dissolve *(24)* in conc. H_2SO_4 followed by dilution with water. The Co—C bond remains intact even under these rather drastic conditions [Eq. (z)][21].

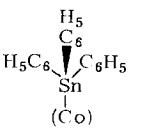


(z)

(24) *(25)*

10.6. Organometallic Derivatives

Cobaloximes with Co—Sn, Co—Ge, Co—Pb, Co—Si, Co—Sb, and Co—Bi bonds were synthesized in 1965 and described in greater detail in 1969[65]. The compound *(26)* is formed by the reaction of cobaloxime(I) with $(C_6H_5)_3SnCl$. It is stable to air and decomposes on reaction with NaOH to yield triphenyltin hydroxide and $(Co^I)^-$; this reaction is reversible. A homolytic cleavage of the Co—Sn bond in *(26)* occurs on irradiation with visible light, the triphenylstannylradical dimerizes to hexaphenyldistannane[67]. Attempts to synthesize analogous compounds of vitamin B_{12} have not yet been successful.



(26)

11. Concluding Remarks

In the present report some of the most important reactions of the cobalt atom in vitamin B_{12} and in cobaloximes have been summarized. Most of the reactions cited may not be surprising to the organic chemist as they are typical for the behavior of organometallic or nucleophilic agents. It is significant, however, that the organometallic derivatives of vitamin B_{12} and those of the model compounds possess both unusual stability *and* reactivity. Vitamin B_{12} appears as an ideally designed biocatalyst; almost all of its complex structural features are necessary to assure high catalytic efficiency and lifetime under enzymatic conditions. The fact that the reactions of cobalt in vitamin B_{12} can be simulated with much simpler compounds is quite surprising, but can be rationalized. Although new reactions of vitamin B_{12} may be discovered in the future, it appears highly probable that the supernucleophilic cobalt(I) derivatives are active forms of vitamin B_{12s} coenzymes.

The results described in the present report were accumulated during the past twelve years. I wish to express my gratitude to my past and present collaborators for their help and contributions.

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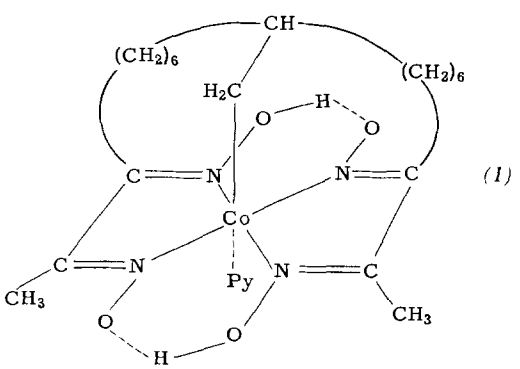
Synthesis and Structure Determination of an Intramolecularly Alkylated Bridged Cobaloxime[**]

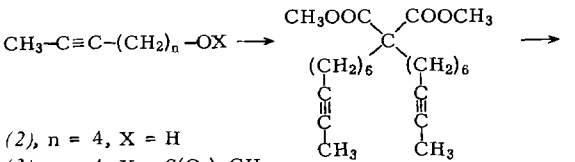
By *Helmut Flohr, Uwe M. Kempe, Wolfgang Pannhorst*, and *János Rétey*[*]

In continuation of our attempts[1,2] to imitate coenzyme B_{12}-dependent enzymatic rearrangements with model catalysts we have synthesized the bridged alkylcobaloxime *(1)*. The starting material employed was 5-heptyn-1-ol *(2)* which is obtainable either by condensation of lithium 1-propyn-1-ide with tetrahydropyranyl 4-bromobutyl ether or by fragmentation of 2,3-epoxy-2-methylcyclohexane tosylhydrazone[3] and subsequent reduction of the resulting aldehyde with $LiAlH_4$.



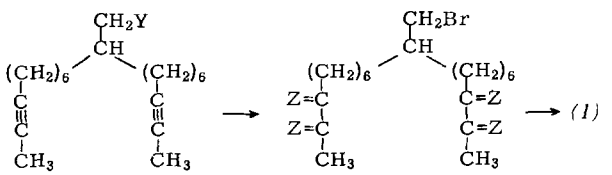
(1)

Compound *(2)* was extended by two C atoms *via* the mesylate *(3)* in a malonic ester synthesis to form 7-nonyn-1-ol *(4)*, the mesylate of which *(5)* could be used for double alkylation of dimethyl malonate. Upon hydrolysis, decarboxylation, and reduction, the bisalkylated malonic ester *(6)* afforded 2-(7-nonynyl)-9-undecyn-1-ol *(7)*, which was converted *via* the mesylate *(8)* into the bromomethyl derivative *(9)*. Ozonization of *(9)* at −18 °C in methanol[4] and subsequent treatment of the peroxide with dimethylsulfide gave the tetraketone *(10)* in 70 % yield. The crystalline tetraoxime *(11)* obtained therefrom was then treated with a stoichiometric amount of cobalt(II) chloride, twice the amount of pyridine, three equivalents of potassium hydroxide, and an excess of $NaBH_4$.



(2), n = 4, X = H
(3), n = 4, X = $S(O_2)$-CH_3
(4), n = 6, X = H
(5), n = 6, X = $S(O_2)$-CH_3

(6)



(7), Y = OH
(8), Y = O-$S(O_2)$-CH_3
(9), Y = Br

(10), Z = O
(11), Z = NOH

The product mixture contained six alkylated cobalt complexes (overall yield *ca.* 20 %) which were separated by thin-layer chromatography. The major product *(1)* [R_f = 0.39, hexane : ethyl acetate : pyridine = 20 : 80 : 1, Merck TLC plate, Kieselgel 60; NMR (270 MHz[5], $CDCl_3$): δ = 0.77—0.92 m; 0.92—1.46 m; 1.46—1.87 m; 1.87—2.05 m; 2.09 d; 2.14 d; 2.17 s (6H); 2.98 d, 3.03 d ($\sum$2H); 7.29 t (2H); 7.69 t (1H); 8.60 d (2H); 18 br. (1H); 18.82 s (1H); UV: λ_{max} = 461 nm (ε = 1190)] was subjected to X-ray diffractometry.

The platelet crystals having a monoclinic habit crystallize from oxydipropionitrile/dichloromethane in the space group $P2_1/c$ with $a = 9.275$, $b = 23.308$, $c = 12.908$ Å, $\beta = 114.48°$; $Z = 4$. Using a Picker diffractometer ($Mo_{K\alpha}$ radiation, graphite monochromator) 4625 symmetrically independent reflections were measured of which 2307 were classified as observed

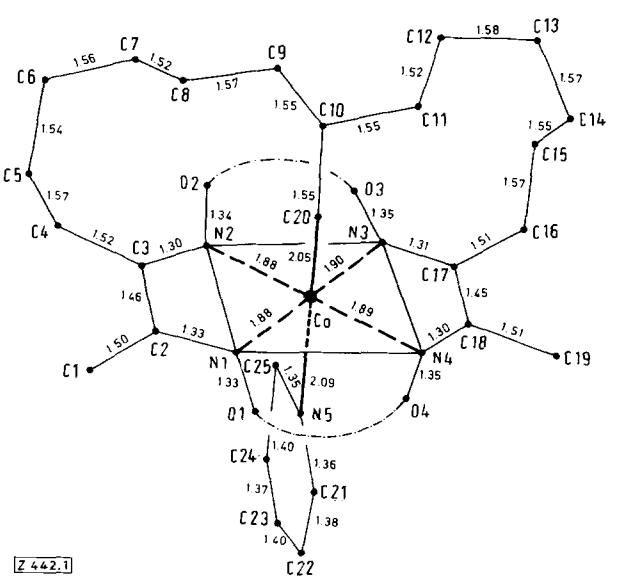


Fig. 1. Structure of the cobaloxime *(1)*. Lengths given in Å.

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$[I_{obs.} \geq 3\sigma(I_{obs.})]$. The positions of the Co atoms were determined by a Patterson synthesis, and those of all the other atoms by difference Fourier synthesis. Refinement of the atomic coordinates and anisotropic temperature factor coefficients for the Co, O, N, and C atoms converged at $R = 0.073$.

The structure found for *(1)* (Fig. 1) does not possess a plane of symmetry; the molecules adopt a chiral conformation. The centrosymmetric unit cell contains four (two sets of two enantiomorphic) molecules. The tertiary H atom in the center of the bridge (on C10) is directed towards the planar ligand system. In this system, which includes the four nitrogen atoms (N1 to N4), the four oxygen atoms, and the eight C atoms (C1 to C4; C16 to C19) the individual atomic nuclei deviate by no more than 0.12 Å from the regression plane. The temperature factor coefficients determined indicate that the bridging C atoms (C3 to C17) are ordered in the crystal lattice and that the bridge is comparatively rigid. This contrasts with the structure of the bridged but not intramolecularly alkylated cobaloxime[6].

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CAS Registry numbers:
(1), 58958-38-6; *(2)*, 58944-42-6; *(3)*, 58944-43-7; *(4)*, 58944-44-8; *(5)*, 58944-45-9; *(6)*, 58944-46-0; *(7)*, 58944-47-1; *(8)*, 58944-48-2; *(9)*, 58944-49-3; *(10)*, 58944-50-6; *(11)*, 58944-51-7

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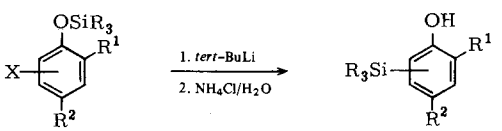
Anionic O→C Rearrangements in Trialkylsiloxybenzenes and Trialkylsiloxypyridines[**]

By *Gerhard Simchen* and *Jörg Pfletschinger*[*]

During studies of *C*-trialkylsilylation reactions[1] we have found that, after prior metalation with *tert*-butyllithium in tetrahydrofuran, bromine-substituted trialkylphenoxysilanes *(1)* rearrange under very mild conditions to trialkylsilylphenols *(2)* (Table 1). After the rearrangement the trialkylsilyl group occupies the position of the halogen.



(1) *(2)*

The reaction proceeds *via* trialkylsiloxy carbanions *(3)* which are in equilibrium with trialkylsilylphenoxide ions *(4)*. The equilibrium shifts in favor of the *C*-silylation products *(4)* with falling temperature.

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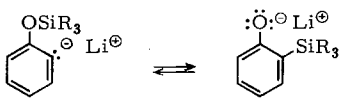
Table 1. Trialkylsilylphenols *(2)* from *(1)*. R_3Si occupies the position of X. Me = CH_3, Et = C_2H_5.

	X	R	R^1	R^2	Conditions T[°C]	Conditions t	Yield [%]	B.p. [°C/torr] m.p. [°C]
a	2-Br	Me	H	H	−30	30 min	76	85/12
b	2-Br	Et	H	H	−30	15 min	97	120/0.05
c	2-Br	Me	H	Me	−30	20 min	93	116/12
d	3-Br	Me	H	H	−30	3 h	80	114/12
e	4-Br	Me	H		25	24 h	85	74
f	4-Br	Me	Me		25	12 h	80	45/0.01
g	4-Br	Et	Me		25	14 h	76	115/0.03

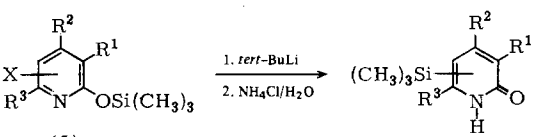
Crossover experiments revealed an intermolecular reaction course for 4-bromotrialkylphenoxysilanes such as *(1e)* and *(1g)*, but an intramolecular mechanism in the case of 2-bromotrialkylphenoxysilanes such as *(1b)* and *(1c)*. Thus a mixture of *(1e)* and *(1g)* gave 19.2% of *(2e)* and 18.3% of *(2g)* together with 25.6% of the crossover products 4-triethylsilylphenol and 18% of *(2f)*. A mixture of *(1b)* and *(1c)* led to 49.5% of *(2b)* and 45.8% of *(2c)*. (Yields determined by gas chromatography.)



(3) *(4)*

In the aliphatic series 1,2-anionic rearrangements with trialkylsilyl shifts are known for benzyl trialkylsilyl ethers[2], and 1,3-anionic rearrangements for hexamethyldisiloxane[3]. Mercuric iodide catalyzes the rearrangement of *O*-alkyl-*O*-trimethylsilylketene acetals to α-trimethylsilyl carboxylic esters[4].

While rearrangement experiments with naphthalene derivatives were not very transparent, the reaction can be extended without difficulty to 3-, 5-, and 6-bromo-2-trimethylsiloxypyridines *(5)* (Table 2).



(5) *(6)*

Table 2. Trimethylsilyl-2-pyridones *(6)* from *(5)*. $(CH_3)_3Si$ occupies the position of X. Me = CH_3, Ph = C_6H_5.

	X	R^1	R^2	R^3	Conditions T[°C]	Conditions t [h]	Yield [%]	M.p. [°C]
a	3-Br		H	H	25	24	62	101—102
b	5-Br	H	H	H	25	18	51	91—93
c	5-Br	Me	H	H	25	20	98	151—153
d	5-Br	H	H	Me	25	42	47	191—194
e	6-Br	H	Ph		25	22	69	210—212

General procedure:

tert-Butyllithium (20 mmol, as 15% solution in *n*-pentane) is added to *(1)* (10 mmol) in anhydrous tetrahydrofuran (50—100 ml) at −78°C with stirring under very pure nitrogen. After reaction under the conditions listed in Tables 1 and 2 the reaction mixture is hydrolyzed with 20% ammonium chloride solution (100 ml), the phases separated, the non-aqueous phase dried over sodium sulfate, the solvent removed under reduced pressure in a rotary evaporator, and the residue fractionated. In the reaction with pyridines the crude product

is not fractionated but instead dissolved in ether, filtered, and, after removal of the ether, recrystallized from acetonitrile or vacuum sublimed.

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German version: Angew. Chem. 88, 444 (1976)

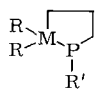
CAS Registry numbers:
(1a), 36601-47-5; *(1b)*, 18032-39-8; *(1c)*, 58933-92-9; *(1d)*, 36971-28-5; *(1e)*, 17828-44-3; *(1f)*, 58933-93-0; *(1g)*, 58933-94-1; *(2a)*, 15288-53-6; *(2b)*, 58933-95-2; *(2c)*, 58933-96-3; *(2d)*, 17881-95-7; *(2e)*, 13132-25-7; *(2f)*, 58933-97-4; *(2g)*, 58933-98-5; *(5a)*, 58933-99-6; *(5b)*, 58934-00-2; *(5c)*, 58934-01-3; *(5d)*, 58934-02-4; *(5e)*, 58934-03-5; *(6a)*, 17379-48-5; *(6b)*, 17379-47-4; *(6c)*, 58934-04-6; *(6d)*, 58934-05-7; *(6e)*, 58934-06-8

[1] *J. Pfletschinger*, Dissertation, Universität Stuttgart 1975.
[2] *R. West, R. Lowe, H. F. Stewart*, and *H. Wright*, J. Am. Chem. Soc. *93*, 282 (1971); *R. West* and *A. Wright*, *ibid. 96*, 3214 (1974); *A. Wright* and *R. West*, *ibid. 96*, 3227 (1974).
[3] *G. A. Gornowicz* and *R. West*, J. Am. Chem. Soc. *90*, 4478 (1968); *R. West* and *G. A. Gornowicz*, J. Organomet. Chem. *28*, 25 (1971).
[4] *I. F. Lutsenko, Yu. I. Baukov, G. S. Burlachenko*, and *B. N. Khasapov*, J. Organomet. Chem. *5*, 20 (1966).

Inversion at Phosphorus in Sila-, Germa-, and Stannaphospholanes[**]

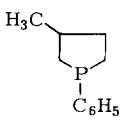
By *C. Couret, J. Escudié, J. Satgé*, and *G. Redoulès*[*]

We recently reported the synthesis of the first sila-, germa-, and stannaphospholanes *(1)*[1]. The 2,2-dimethyl-1-phenyl derivatives *(2)* of these compounds are particularly well suited for dynamic NMR investigations, since the diastereotopic methyl groups give rise to two very pronounced doublets in the NMR spectrum (Table 1).



(1): M = Si, Ge, Sn
R = Me, Et, Ph
R′ = *n*-Bu, Ph

(2a): M = Si, R = Me, R′ = Ph
(2b): M = Ge, R = Me, R′ = Ph
(2c): M = Sn, R = Me, R′ = Ph



(3)

Table 1. Physical properties of compounds *(2)* and *(3)*.

Cpd.	δMe¹ [ppm]	*J*(P—Me¹) [Hz]	δMe² [ppm]	*J*(P—Me²) [Hz]	Coalescence temperature [°C]	$\Delta G^{\neq}$ [kcal/mol]	Electronegativity [3]
(2a)	−0.14 (d) [a]	1.7	0.34 (d) [a]	7.5	140	21.3	Si: 1.90
(2b)	0.05 (d) [a]	1.75	0.50 (d) [a]	5.25	200	24.3	Ge: 2.01
(2c)	0.02 (d) [b]	1.5	0.42 (d) [b]	2.25	155	21.95	Sn: 1.96
(3)						36 [2]	C: 2.55

[a] In [D_6]-acetone *vs.* tetramethylsilane as internal standard.
[b] Neat, *vs.* tetramethylsilane as internal standard.

We have determined the coalescence temperatures of compounds *(2)* and calculated the free energy of activation $\Delta G^{\neq}$ for inversion using the Eyring equation:

$$\Delta G^{\neq} = 4.57\, T_c \left(9.97 + \log \frac{T_c}{\Delta \nu}\right)$$

(T_c = coalescence temperature, $\Delta\nu$ = maximum difference between the chemical shifts of the methyl groups). The results are listed in Table 1. *Mislow et al.*[2] have determined a free activation energy of 36 kcal/mol for inversion in the metal-free phospholane *(3)*.

As can be seen from Table 1, there is an almost linear relationship between the free energy of activation of inversion at the phosphorus atom and the electronegativity[3] of the neighboring metal or carbon atoms. These results are in agreement with the observations by *Mislow et al.*[4] on the corresponding open-chain phosphanes.

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CAS Registry numbers:
(2a), 54770-04-6; *(2b)*, 54770-07-9; *(2c)*, 54770-39-7

[1] *C. Couret, J. Escudié, J. Satgé*, and *G. Redoulès*, C.R. Acad. Sci., Ser. C, *279*, 225 (1974).
[2] *W. Egan, R. Tang, G. Zon*, and *K. Mislow*, J. Amer. Chem. Soc. *92*, 1442 (1970).
[3] *A. L. Allred* and *E. G. Rochow*, J. Inorg. Nucl. Chem. *5*, 269 (1958); *A. L. Allred*, *ibid. 17*, 215 (1961).
[4] *R. D. Baechler* and *K. Mislow*, J. Amer. Chem. Soc. *93*, 773 (1971).

Optically Active Bridgehead Derivatives of Trishomobarrelene and Trishomobullvalene[**]

By *Werner Spielmann* and *Armin de Meijere*[*]

Bridgehead derivatives of trishomobarrelene *(1a)*[1] and of trishomobullvalene *(2a)*[1a] as well as the unsubstituted hydrocarbon *(2a)* itself possess C_3 symmetry and are consequently chiral. Such optically active compounds are of interest in connection with the question whether, and if so to what extent, the propeller structure of the carbon skeleton makes a significant contribution to the chiroptical properties.

Optically active compounds *(1)* and *(2)* are accessible by resolution of the racemic carboxylic acids *(1b)* and *(2b)*, respectively. Resolution of the diastereomeric salts with

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[**] The authors wish to thank Professor *K. Mislow* for critical examination of the manuscript and Dr. *J. Parello*, Montpellier University, for his participation in the NMR investigation of the germaphospholane *(2b)*.

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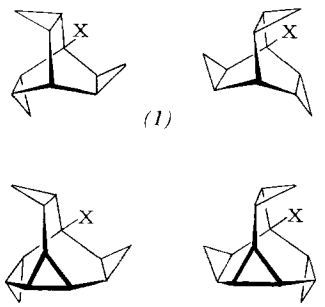
[**] Presented in part at the "Chemiedozententagung" (April 1975) at Düsseldorf and the Eleventh Euchem Bürgenstock Stereochemistry Conference (April/May 1975).—This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, BASF AG, and Deutsche Shell-Chemie GmbH.

quinine afforded levorotatory material in both cases. Use of D-(+)-α-phenylethylamine led in the case of *(1b)* to enrichment of the (+)-enantiomer, but to enrichment of the (−)-enantiomer in the case of *(2b)*. Dextrorotatory carboxylic acid *(2b)* was obtained using L-(−)-α-phenylethylamine as the optically active auxiliary base.



(1)

(2)

(a), X = H
(b), X = CO_2H
(c), X = Cl
(d), X = OH
(e), X = OAc
(f), X = D
(g), X = ⊕

The maximum rotation of *(1b)* and *(2b)* could be established for the [carbonyl-^{14}C]-carboxylic acids by means of the isotopic dilution method[2]. It could be estimated from the maximum rotations (Table 1) that in the most favorable case *(1b)* was obtained in 72 to 73% optical purity with D-(+)-α-phenylethylamine and *(2b)* in 98 to 99% optical purity with quinine.

Table 1. Maximum specific rotations $[\alpha_{max}]_D^{20}$ [°] of optically active trishomobarrelene *(1)* and trishomobullvalene derivatives *(2)*.

	X	*(1)* $[\alpha_{max}]_D^{20}$ [a]	*(2)* $[\alpha_{max}]_D^{20}$ [a]
a	H	0	+ 117±3 (CCl_4)
b	CO_2H	+ 125 ± 3 (EtOH)	+ 233± 4 (EtOH)
c	Cl	+ 159 ± 4 (CH_2Cl_2)	+ 273±5 (CCl_4)
d	OH	+ 70 ±2 (CH_2Cl_2)	+ 250± 5 (CCl_4)
e	OAc	+ 103 ± 4 (CH_2Cl_2)	—
f	D	− 1.2 (CCl_4)	—
g	⊕	−1516 ±40 (CH_2Cl_2) [b]	−2473±53 (CH_2Cl_2) [b]

[a] Relative direction of rotation based on the (+)-carboxylic acid; average values of several measurements at concentrations $c = 0.3-0.7$ g/100 ml.
[b] Measured at −50°C.

Starting from the optically active carboxylic acids it proved possible to prepare the optically active compounds *(1c)*—*(1f)* as well as *(2a)*, *(2c)*, and *(2d)* (Table 1). Thus the reaction of (+)-*(1b)* and (+)-*(2b)* with lead tetraacetate in the presence of *N*-chlorosuccinimide[3] gave the dextrorotatory bridgehead chlorides (+)-*(1c)* and (+)-*(2c)*, respectively. The bridgehead acetates (+)-*(1e)* and (+)-*(2e)*, of which only (+)-*(1e)* was isolated, were formed as by-products.

Reduction of the (+)-chlorides *(1c)* and *(2c)* with $LiAlD_4$ and $LiAlH_4$ furnished the optically active hydrocarbons [1-D]-trishomobarrelene (−)-*(1f)* and trishomobullvalene (+)-*(2a)*, respectively. Hydrolysis of the (+)-chlorides in aqueous dioxane gave the optically active alcohols (+)-*(1d)* and (+)-*(2d)*.

The exceptional stability of the bridgehead carbenium ions of trishomobarrelene and trishomobullvalene[4] prompted us to attempt generation of the free optically active cations *(1g)* and *(2g)*. On reaction of the chlorides (+)-*(1c)* and (+)-*(2c)* in dichloromethane with antimony pentafluoride at −78°C (cf. ref.[4b]) clear pale yellow solutions were obtained. The two (+)-chlorides afforded carbenium ion solutions displaying negative rotations with surprisingly high rotatory powers (cf. Table 1). The specific rotations of the solutions did not change within 1 to 2 h at −50°C; addition of water gave (+)-*(1d)* and (+)-*(2d)* from which (+)-*(1c)* and (+)-*(2c)* could be regenerated in unchanged optical purity by reaction with thionyl chloride and concentrated hydrochloric acid, respectively. Thus neither *(1g)* nor *(2g)* racemizes under these conditions, although this would be feasible by an intermolecular hydride exchange with the second bridgehead of the molecule in the case of *(1g)*. It appears that this process is not suppressed for steric reasons[5] but rather because intermediate formation of a 1,5-trishomobarrelenylene dication would be required.

The chiral skeletons of *(1)* and *(2)* each contain six chiral centers. Calculations with the aid of *Brewster*'s conformation dissymmetry model[6] permit prediction of the (all-*S*) configuration for the dextrorotatory derivatives *(1b)*—*(1d)*, *(2b)*—*(2d)*, and for (−)-*(1f)*[7]. Assuming that this model[6] correctly reproduces the direction of rotation of compounds *(1)* and *(2)* for a given configuration, a comparison of the calculated and experimental molar rotations becomes informative (Table 2).

Table 2. Calculated [6] and experimental molar rotations [°] of (2*S*,4*S*,6*S*,8*S*,9*S*,11*S*)-1-trishomobarrelene *(1)* and (2*S*,4*S*,8*S*,10*S*,11*S*,13*S*)-1-trishomobullvalene derivatives *(2)*. The direction of rotation is given relative to the (+)-carboxylic acids assuming them to possess the (all-*S*)-configuration.

	X	$[M]_{calc}$	$[M]_{exp}$	$[M]_{exp}-[M]_{calc}$
(1a)	H [a]	0	0	0
(1b)	CO_2H	+260	+238	− 22
(1c)	Cl	+443	+286	−157
(1d)	OH	+ 69	+113	+ 44
(1f)	D	− 4	− 1.8	+ 2.2
(2a)	H [b]	0	+201	+201
(2b)	CO_2H	+260	+503	+243
(2c)	Cl	+443	+562	+119
(2d)	OH	+ 69	+470	+401

[a] (2*S*,4*R*,6*R*,8*S*,9*S*,11*R*)-configuration.
[b] (2*S*,4*R*,8*R*,10*S*,11*S*,13*R*)-configuration.

It is striking that the values $[M]_{exp}-[M]_{calc}$ for *(2)* are all positive, while they are negative or only just positive for *(1)*. Thus it is suspected that, at least in the case of the trishomobullvalene system *(2)*, the chiral propeller structure of the carbon skeleton makes a significant contribution to the overall rotation. In particular, the pronounced rotation of the hydrocarbon *(2a)*—it contains three (*S*)- and three (*R*)-configurated chiral centers and is predicted by the model to display no rotation—could only be explained in this manner. Accordingly, *(2a)* and especially also the free cations *(1g)* and *(2g)* with their high rotatory powers are suitable test cases for advanced models of optical activity[8] and chirality functions[9].

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CAS Registry numbers:
racemic-(1b), 59284-86-5; (+)-*(1b)*, 59246-21-8; (−)-*(1b)*, 59246-22-9; (+)-*(1c)*, 59246-23-0; (+)-*(1d)*, 59187-61-0; (+)-*(1e)*, 59187-62-1; (−)-*(1f)*, 59246-24-1; (−)-*(1g)*, 59284-82-1; (+)-*(2a)*, 59246-25-2; *racemic-(2b)*, 59246-26-3; (+)-*(2b)*, 59246-27-4; (−)-*(2b)*, 59246-28-5; (+)-*(2c)*, 59246-29-6; (+)-*(2d)*, 59203-48-4; (+)-*(2e)*, 59169-65-2; (−)-*(2g)*, 59203-49-5; quinine, 130-95-0; D-(+)-α-phenylethylamine, 3886-69-9; L-(−)-α-phenylethylamine, 2627-86-3

[1] a) *A. de Meijere* and *C. Weitemeyer*, Angew. Chem. *82*, 359 (1970); Angew. Chem. Int. Ed. Engl. 9, 376 (1970); b) *A. de Meijere*, *O. Schallner*, and *C. Weitemeyer*, Tetrahedron Lett. *1973*, 3483.
[2] For method, see *H. Gerlach*, Helv. Chim. Acta *49*, 2481 (1966).
[3] *K. B. Becker*, *M. Geisel*, *C. A. Grob*, and *F. Kuhnen*, Synthesis *1973*, 493.
[4] a) *A. de Meijere*, *O. Schallner*, and *C. Weitemeyer*, Angew. Chem. *84*, 63 (1972); Angew. Chem. Int. Ed. Engl. *11*, 56 (1972); b) *A. de Meijere* and *O. Schallner*, *ibid. 85*, 400 (1973) and *12*, 399 (1973), respectively.
[5] Hydride abstraction from *(2a)* by *(1g)* to form the cation *(2g)* and the hydrocarbon *(1a)* has been observed. *W. Spielmann* and *A. de Meijere*, unpublished results.

[6] *J. H. Brewster*, J. Am. Chem. Soc. *81*, 5475, 5483, 5493 (1959); Tetrahedron *13*, 106 (1961).
[7] The absolute configurations of compounds *(1)* and *(2)* are unknown; an X-ray structural study of *(1c)* is in progress.
[8] *J. H. Brewster*, Top. Curr. Chem. *47*, 29 (1974).
[9] *E. Ruch*, Acc. Chem. Res. *5*, 49 (1972).

Four Linearly Annelated Cyclobutane Rings: The Tetracyclo[4.4.0.0^{2,5}.0^{7,10}]decane System[**]

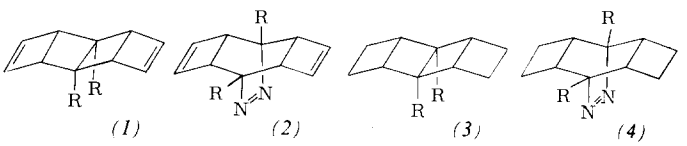
By *Hans-Dieter Martin* and *Mirko Hekman*[*]

We recently reported the synthesis[1] of pterodactyladiene *(1)*, a highly strained representative of the $(CH)_{10}$ isomers. In the present communication we now report:

a) The preparation and an unexpected thermal isomerization of pterodactylane *(3)*, the course of which has been established by isotopic labeling.

b) The elucidation of the mechanism of thermolysis of *(1)*.

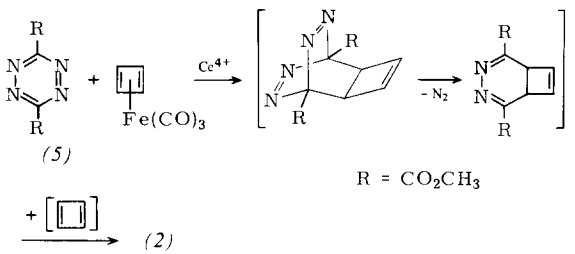
c) The synthesis and thermolysis of the azo compounds *(2)* and *(4)*. Compound *(2)* provides an entry to the $(CH)_{10}$ energy surface which is distinct from *(1)* and permits a decision between the various reaction pathways proposed for *(1)*.



(1) *(2)* *(3)* *(4)*

R = CO_2CH_3

Reaction of cyclobutadienetricarbonyliron and ammonium cerium(IV) nitrate with the 3,6-disubstituted *s*-tetrazine *(5)* at 0 °C affords *(2)*, m.p. 103—105 °C. Heating of *(2)* in per-

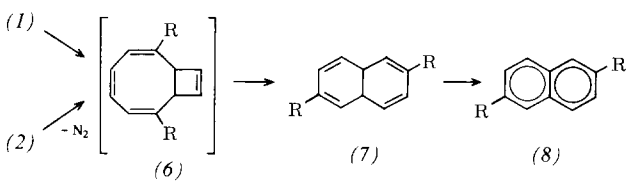


(5)

R = CO_2CH_3

(2)

chlorobutadiene (2 h, 140 °C) gives the naphthalene *(8)* almost quantitatively. Transient formation of 4a,8a-dihydronaphthalene *(7)*[1] can be detected by NMR spectroscopy.



(6) *(7)* *(8)*

R = CO_2CH_3

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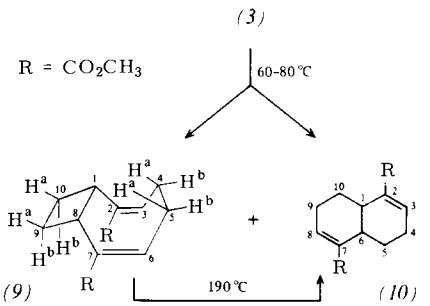
The fact that *(1)* and *(2)* both give the same product *(7)* shows the first step of thermolysis of *(1)* to be rupture of the central strained bond (path A in ref. [1]). A bicyclo[6.2.0]-decatetraene *(6)* which is unstable under the reaction conditions has been proposed as the first intermediate *en route* from *(1)* to *(7)*. Its tetrahydro derivative *(9)*, which is no longer accessible to electrocyclic ring opening to form a cyclodecapentaene, should be isolable. The behavior of compound *(3)*, from which *(9)* could be formed thermally, therefore attracted our interest.

Thermolysis of pterodactylane *(3)*, m.p. 57—60 °C, prepared from *(1)* by hydrogenation (Pd/C in CH_3OH), in boiling CCl_4 gives not only *(9)* but also surprisingly compound *(10)* (ratio 1 : 1).

The structures *(9)* and *(10)* are based on spectral data, on the oxidative degradation of *(9)* with ozone or $KMnO_4/KIO_4$, which leads to succinic acid, and on the dehydrogenation of *(10)* with dichlorodicyanoquinone (DDQ) to dimethyl 1,5-naphthalenedicarboxylate.



(3)

R = CO_2CH_3

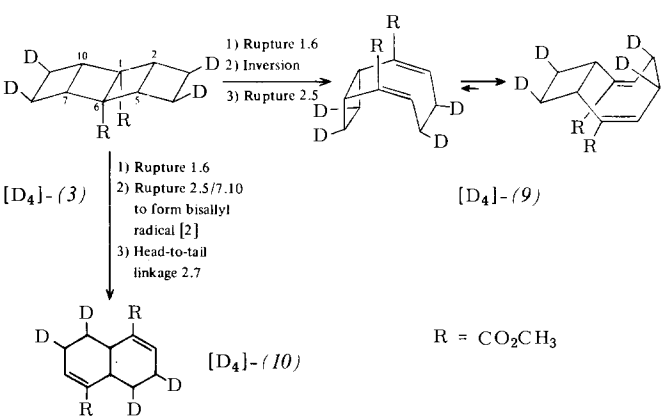
60-80 °C

(9) *(10)*

190 °C

The transformation of *(9)* to *(10)* only at temperatures of about 190 °C shows that *(10)* cannot be regarded as a product of *(9)* under the given reaction conditions (60—80 °C). Rather both *(9)* and *(10)* are formed directly from *(3)*.

The thermolysis of tetradeuteriated *(3)* furnishes evidence for the reorganization of the molecule and for the formation pathway of *(9)* and *(10)*. In $[D_4]$-*(9)* the deuterium occupies the positions 4a,5a,9a, and 10a, and in $[D_4]$-*(10)* positions 4, 5, 9, and 10. The site of deuteriation in *(3)* follows from the NMR spectra of *(3)* and $[D_4]$-*(3)* in the presence of a shift reagent.



1) Rupture 1.6
2) Inversion
3) Rupture 2.5

$[D_4]$-*(3)*

1) Rupture 1.6
2) Rupture 2.5/7.10 to form bisallyl radical [2]
3) Head-to-tail linkage 2.7

$[D_4]$-*(9)*

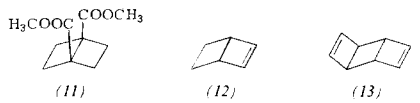
$[D_4]$-*(10)*

R = CO_2CH_3

The azo compound *(4)*, m.p. 160—162 °C, prepared by diimide reduction of *(2)* (potassium azodicarboxylate and acetic acid at 0 °C) affords *(9)* as major product accompanied by only about 5% of *(10)* on thermolysis. This product distribution is in accord with results obtained for other azo compounds[3].

The kinetic parameters of *(1)*, *(3)*, *(11)*, *(12)*, and *(13)* (Table 1) confirm the uniform mechanism, which is initiated

by cleavage of the central σ-bond; comparison with *(12)* and *(13)* rules out a primary cyclobutene ring opening as (proposed[1]) alternative mechanism in the case of *(1)*. Annelated cyclobutane or cyclobutene rings such as those in *(3)* and *(1)* therefore have practically no influence on the Arrhenius parameters of *(11)*.



(11) *(12)* *(13)*

Table 1. Kinetic data. G = gas phase, L = liquid phase.

Compound		E_a [kcal/mol]	log A	Ref.
(1)	L	24.5	12.0	[1]
(3)	L	24.1	11.9	this communication
(11)	L	25.5	12.1	this communication, [4]
(12)	L	31.7	13.6	this communication
(13)	G	32.6	14.0	[5]
		32.4	14.2	[6]

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in abridged form: April 1, 1976 [Z 452 IE]
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CAS Registry numbers:
(1), 49542-83-8; *(2)*, 59247-30-2; *(3)*, 59247-31-3; *(4)*, 59247-32-4; *(5)*, 2166-14-5; *(7)*, 59247-33-5; *(8)*, 840-65-3; *(9)*, 59247-34-6; *(10)*, 59247-35-7; *(11)*, 31947-22-5; *(12)*, 3097-63-0; cyclobutadienetricarbonyliron, 12078-17-0

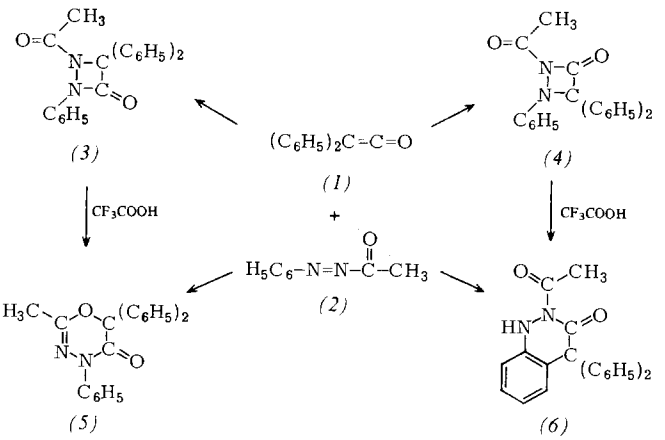
[1] *H.-D. Martin* and *M. Hekman*, Angew. Chem. *85*, 615 (1973); Angew. Chem. Int. Ed. Engl. *12*, 572 (1973).
[2] The fragmentation of a 1,4-cyclohexanediyl into two allyl radicals is endothermic to the extent of about 25 kcal/mol; however, annelation of two four-membered rings (strain energy 52 kcal/mol) can lead to exothermic cleavage. The formation of an intermediate *trans,trans*-diene from *(3)* as a precursor of *(10)* has been suggested as an interesting alternative by *H. Schmid*.
[3] *L. A. Paquette, M. R. Short*, and *J. F. Kelly*, J. Am. Chem. Soc. *93*, 7179 (1971); *W. R. Roth* cited in *J. K. Kochi*: Free Radicals. Vol. I, Wiley-Interscience 1973, p. 229; *W. R. Roth* and *M. Martin*, Tetrahedron Lett. *1967*, 3865. The equilibration of intermediate nitrogen-free fragments, as observed in the case of diazabicyclo[2.2.2]octenes, possibly does not occur here.
[4] The kinetics of thermolysis of *(11)* was investigated in collaboration with Dr. *Daniel Bellus*, Basel.
[5] *H. M. Frey, H.-D. Martin*, and *M. Hekman*, J. Chem. Soc. Chem. Commun. *1975*, 204.
[6] *R. S. Case, M. J. S. Dewar, S. Kirschner, R. Pettit*, and *W. Slegier*, J. Am. Chem. Soc. *96*, 7581 (1974).

Competing Cycloadditions in the Reaction of Acetylazobenzene with Diphenylketene

By *Sven Sommer*[*]

Among the few cycloadditions undergone by aryl azo compounds of the type Ar—N=N—X [X = Ar, $CH(CH_3)_2$, $N(CH_3)_2$, $CO_2C_2H_5$, C≡N] are to be found the reactions with diphenylketene *(1)*[1-3]. Only [2+2] cycloadducts (1,2-diazetidinones) have so far been isolated as reaction products. In contrast, the reaction of acetylazobenzene *(2)* with *(1)* (1:1 in benzene at room temperature) leads to the two [2+2] cycloadducts *(3)* and *(4)*, to a [4+2] cycloadduct *(5)*, and to a product *(6)* formally arising by [4+2] cycloaddition and subsequent 1,3-H shift.

No mutual interconversion of the products under the reaction conditions could be detected. It is remarkable that in



spite of the considerable difference in electronic character of the substituents attached to the azo group both regioisomers *(3)* and *(4)* should be formed. In contrast, the comparable reactions of arylazonitriles[3] and ethyl benzeneazocarboxylate[2, 4] with *(1)* were found to give only one 1,2-diazetidinone of type *(3)* in each case.

The exothermic reaction of *(1)* with *(2)* is complete within *ca.* 1 h; the ^{1}H-NMR spectrum of the crude solution shows it to proceed quantitatively. Compounds *(3)* and *(4)* are isolated by fractional crystallization from methanol. Pure *(5)* and *(6)* can be obtained by rearrangement of *(3)*[5] and *(4)*, respectively, under the influence of trifluoroacetic acid. Crystalline *(5)* and *(6)* are also obtained on seeding the reaction solution after extensive removal of *(3)* and *(4)*. The structures of *(3)* and *(5)* have been proved by independent syntheses[2, 6], and the structures of *(4)* and *(6)* by IR, ^{1}H-NMR, and ^{13}C-NMR spectra (Table 1).

Table 1. Cycloadducts from diphenylketene *(1)* and acetylazobenzene *(2)*. All compounds gave correct CHN analyses. The product composition was determined from the integrals of the methyl signals in the ^{1}H-NMR spectrum of the crude solution.

Cpd.	M.p. [°C]	^{1}H-NMR [a] δCH_3	IR [cm^{-1}] [KBr] νC=O (Ring)	νC=O	Proportion [%]
(3)	171 [b] 169—170 [2]	1.65	1792	1709	60
(4)	167—168 [b]	2.50	1796	1725	26
(5)	136—137 [b] 136 [6]	2.08	1678	(νC=N =1660)	10
(6)	182—183 [c]	2.67 (δNH =8.43)	1680 (νNH =3280)	1715	4

[a] δ-values [ppm], in $CDCl_3$ with TMS as internal standard.
[b] From methanol.
[c] Dissolved in ethyl acetate and precipitated with methanol.

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German version: Angew. Chem. *88*, 449 (1976)

CAS Registry numbers:
(1), 525-06-4; *(2)*, 13443-97-5; *(3)*, 59231-00-4; *(4)*, 59231-01-5; *(5)*, 59231-02-6; *(6)*, 59231-03-7

[1] *R. C. Kerber, T. J. Ryan*, and *S. D. Hsu*, J. Org. Chem. *39*, 1215 (1974).
[2] *C. W. Bird*, J. Chem. Soc. *1963*, 674.
[3] *C. W. Bird*, J. Chem. Soc. *1964*, 5285.
[4] On the basis of a shoulder at *ca.* 1820 cm^{-1} in the IR spectrum of the crude solution, *Kerber et al.* [1] suspect the formation of small amounts of the regioisomer of type *(4)*; confirmatory evidence and an isolation have yet to be reported.
[5] The rearrangement *(3)* → *(5)* has already been performed with the aid of concentrated HCl. Under these conditions *(5)* is formed together with two other products in only 23% yield [2]. In trifluoroacetic acid the rearrangements *(3)* → *(5)* and *(4)* → *(6)* are quantitative.
[6] *J. van Alphen*, Rec. Trav. Chim. Pays-Bas *48*, 163 (1929).

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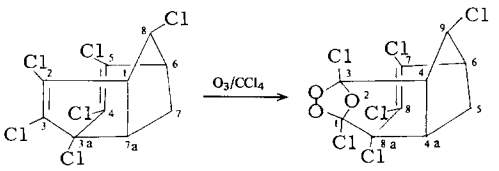
Ozonolysis of 2,3,3a,4,5,8-Hexachloro-3a,6,7,7a-tetrahydro-1,6-methano-1*H*-indene: Isolation of a Stable Ozonide Having a 3,5-Dichloro-1,2,4-trioxolane Structure

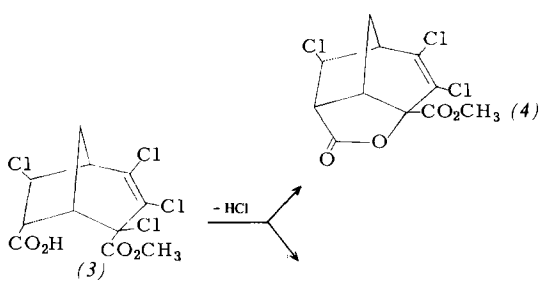
By *Siegmar Gäb*, *Siegfried Nitz*, *Harun Parlar*, and *Friedhelm Korte*[*]

Whereas numerous stable monomeric ozonides (1,2,4-trioxolanes) are known[1] no defined addition compounds have yet been reported between ozone and chlorinated olefins[2]. On reaction of 2,3,3a,4,5,8-hexachloro-3a,6,7,7a-tetrahydro-1,6-methano-1*H*-indene *(1)*[3] with ozone in carbon tetrachloride we have now succeeded in isolating a compound having a 3,5-dichloro-1,2,4-trioxolane structure.

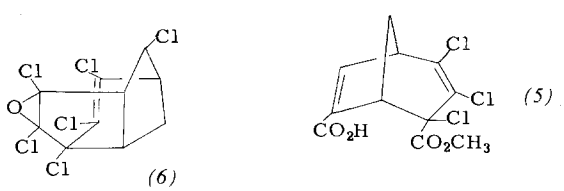


(1) *(2)*

The colorless product 1,3,7,8,8a,9-hexachloro-4a,5,6,8a-tetrahydro-1,3-epidioxy-4,6-methanoisochromane *(2)*, m.p. 100—101 °C, is stable at room temperature. Slow decomposition only occurs on exposure to moisture. Reductive opening with KI in methanol affords the monomethyl ester *(3)*. The structural assignment of *(2)* is based on spectroscopic data and on structural analysis of *(3)* and its dehydrohalogenation products *(4)* and *(5)*[4].



(3) *(4)*



(6) *(5)*

The ^{13}C-NMR data of the epoxide *(6)*[5] show that compound *(2)* is not a primary ozonide.

Procedure:

A solution of *(1)* (1 g) in CCl_4 (100 ml) is ozonized at room temperature until a blue coloration is observed. After 2 h excess ozone is driven off with N_2 and the solvent removed under reduced pressure. The oily residue is purified by column chromatography on silica gel (light petroleum) and recrystallized from *n*-hexane. Yield: 0.85 g (75 %) of *(2)*.

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CAS Registry numbers:
(1), 56641-38-4; *(2)*, 59473-46-0; ozone, 10028-15-6

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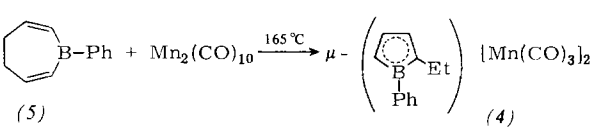
[1] *R. Criegee*, Angew. Chem. *87*, 765 (1975); Angew. Chem. Int. Ed. Engl. *14*, 745 (1975), and references cited therein.
[2] *K. Griesbaum* and *J. Brüggemann*, Chem. Ber. *105*, 3638 (1972); *K. Griesbaum* and *P. Hofmann*, J. Am. Chem. Soc., in press.
[3] Brit. Pat. 946079 (1964), Velsicol Chemical Corp.; Chem. Abstr. *60*, 9167f (1964); *S. Gäb, H. Parlar, W. P. Cochrane, H. G. Fitzky, D. Wendisch*, and *F. Korte*, Liebigs Ann. Chem. *1976*, 1.
[4] Reaction of *(2)* with KI in CH_3OH gives *(3)* and *(4)* in the ratio 1 : 1.5. Compound *(3)* is quantitatively converted into *(4)* by chromatography on silica gel. Heating of an acetone solution of *(3)* to *ca.* 50 °C gives exclusively compound *(5)*.
[5] Compound *(6)* is produced by reaction of *(1)* with CrO_3 in glacial acetic acid.

A Novel Type of Triple-Decker Complex—Borole as Bridging Ligand[1]

By *Gerhard E. Herberich*, *Joachim Hengesbach*, *Ulrich Kölle*, *Gottfried Huttner*, and *Albin Frank*[*]

Three triple-decker sandwich complexes have so far been reported, namely the $[Ni_2(C_5H_5)_3]^+$ ion[2] *(1)* and two isomers $(\mu\text{-L})Co_2(C_5H_5)_2$[3] *(2)* and *(3)* with planar L = 1,2,3-$C_2B_3H_5$ and 1,2,4-$C_2B_3H_5$, respectively.

We have now found a novel type of triple-decker complex[4] in the form of μ-(1-phenyl-2 ethylborole)bis(tricarbonylmanganese) *(4)*. Surprisingly, *(4)* is formed as main product in the reaction of 1-phenyl-4,5-dihydroborepin[5] *(5)* with $Mn_2(CO)_{10}$ in boiling mesitylene. The *central* ligand is a simple borole derivative[6] which acts as a bridge between two Mn atoms each with three CO groups as *outer* ligands.



(5) *(4)*

The composition of complex *(4)* follows from elemental analysis and the mass spectrum [*m/e* 446 (26 %; $M^+ \equiv LMn_2(CO)_6^+$), successive loss of six CO groups, 278 (87 %; LMn_2^+), 223 (37 %; LMn^+), 55 (100 %; Mn^+)]. The ^{1}H-NMR spectrum reveals the borole ring [τ values in C_6D_6 at 100 MHz and room temperature; Ph: 2.43 m (2H), 2.66 m (3H); H-5: 5.76 t (1H); H-4: 6.43 dd (1H); H-3: 7.84 dd (1H); $J_{34} = 3.7$, $J_{45} = 1.8$ and $J_{35} = 1.3$ Hz; Et: 8.19 q (2H), 9.23 t (3H), $J = 7.3$ Hz], the ^{11}B-NMR spectrum the B atom bound to Mn [δ value in C_6D_6 at room temperature: −17.6 ppm rel. to $BF_3 \cdot OEt_2$ (ext.)]. The IR spectrum shows the typical pattern of a $Mn(CO)_3$ group in an environment deviating strongly from C_{3v} symmetry [ν_{CO} (cm^{-1}) in hexane: 2022 vs, 1963 vs, 1952 vs]; no indications of an interaction between the two $Mn(CO)_3$ groups in the molecule are observed. The constitution of *(4)* cannot be trivial, since apparently a four-electron ligand has substituted four (!) CO groups of $Mn_2(CO)_{10}$. Though the data quoted are in accord with

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the triple-decker structure of *(4)*, they do not however provide unequivocal proof thereof. The structure was therefore determined X-ray crystallographically.

$C_{18}H_{13}BMn_2O_6$ *(4)* crystallizes orthorhombically with $a=1429(1)$, $b=1670(1)$, $c=1541(1)$ pm, space group Pbca, $Z=8$. 1113 diffraction data (Syntex-P21) with $I \geq 3.2\sigma$; solution: conventional; refinement: (Syntex-XTL) full matrix, $R_1=0.057$. Figure 1 shows a schematic representation of the molecular structure, the skeletal unit of which is a pentagonal bipyramidal metallocarborane cluster of the *closo* type. The apical positions are occupied by $Mn(CO)_3$ groups; the four carbon atoms and the boron atom of the borole ring occupy the equatorial positions. The disorder which complicates the structural analysis of all previously investigated triple-decker complexes[2b, 3a, 3c] does not occur in the case of *(4)*.

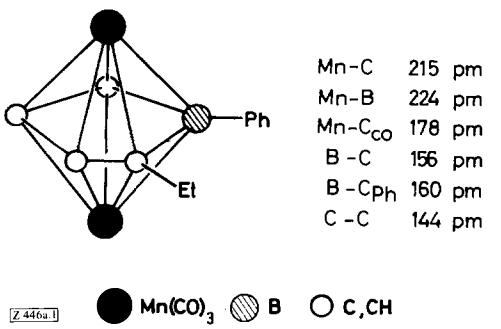

Fig. 1. Molecular structure of the dinuclear borole complex *(4)*.

The bonding in *(4)* is the same as that in metallocarboranes[7]. In a broad sense *(4)* is isoelectronic with *(2)* and *(3)*.

Procedure:

A mixture of *(5)*[5] (1.0 g, 5.95 mmol) and $Mn_2(CO)_{10}$ (2.32 g, 5.95 mmol) in mesitylene (20 ml) is heated under reflux for 70 h. Chromatographic workup (SiO_2-gel with pentane as eluant) affords two main zones: *ca.* 0.45 g (20 %) $Mn_2(CO)_{10}$ and 1.25 g (57 % yield referred to reacted $Mn_2(CO)_{10}$) of *(4)*, m.p. 119—120 °C, no decomposition up to 200 °C. The new complex, which crystallizes from pentane as brown-red needles, is very soluble in CH_2Cl_2, benzene, and acetone, readily soluble in Et_2O, and moderately soluble in pentane. It is somewhat air-sensitive in solution.

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CAS Registry numbers:
(4), 59318-07-9; *(5)*, 59269-92-0; $Mn_2(CO)_{10}$, 10170-69-1; ^{11}B, 14798-13-1

[1] Triple Decker Complexes, Part 1. Based on lectures at Marburg (Jan. 19, 1976) and Regensburg (Feb. 9, 1976).—This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[2] a) *A. Salzer* and *H. Werner*, Angew. Chem. *84*, 949 (1972); Angew. Chem. Int. Ed. Engl. *11*, 930 (1972); *H. Werner* and *A. Salzer*, Synth. Inorg. Met.-Org. Chem. *2*, 239 (1972); b) *E. Dubler, M. Textor, H.-R. Oswald*, and *A. Salzer*, Angew. Chem. *86*, 125 (1974); Angew. Chem. Int. Ed. Engl. *13*, 135 (1974).

[3] a) *D. C. Beer, V. R. Miller, L. G. Sneddon, R. N. Grimes, M. Mathew*, and *G. J. Palenik*, J. Am. Chem. Soc. *95*, 3046 (1973); b) *R. N. Grimes, D. C. Beer, L. G. Sneddon, V. R. Miller*, and *R. Weiss*, Inorg. Chem. *13*, 1138 (1974); c) *W. T. Robinson* and *R. N. Grimes, ibid. 14*, 3056 (1975).

[4] The more restricted designation, "Triple-Decker Sandwich Complexes" is retained for compounds with ring ligands as outer ligands. A complex $L[Mn(CO)_3]_2$ with L = 3,4-diethyl-2,5-dimethyl-1,2,5-thiadiborolene which has recently been prepared ought according to spectroscopic findings to be likewise regarded as a triple-decker complex: *W. Siebert*, private communication, Feb. 24, 1976; *W. Siebert* and *K. Kinberger*, Angew. Chem. *88*, 451 (1976); Angew. Chem. Int. Ed. Engl. *15*, 434 (1976).

[5] *D. Sheehan*, Ph. D., Yale University 1964; Diss. Abstr. *25*, 4417 (1965); cf. also *A. J. Leusink, W. Drenth, J. G. Noltes*, and *G. J. M. van der Kerk*, Tetrahedron Lett. *1967*, 1263.

[6] The only known borole derivative is pentaphenylborole: *J. J. Eisch, N. K. Hota*, and *S. Kozima*, J. Amer. Chem. Soc. *91*, 4575 (1969).

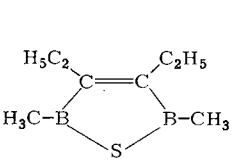
[7] *K. Wade*, Chem. Brit. *11*, 177 (1975); and literature cited therein. Alternatively the central borole ring can be regarded as a doubly negative anionic 6π electron system; both Mn atoms then complying with the noble gas rule.

Thiadiborolenebis(tricarbonylmanganese)—A Cluster with Triple-Decker Structure[1]

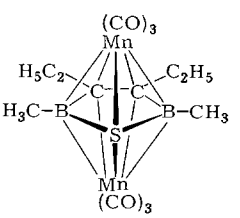
By *Walter Siebert* and *Klemens Kinberger*[*]

The 1,2,5-thiadiborolene *(1)* reacts with metal carbonyls to give the *nido* compounds $[(1)\cdot Cr(CO)_4]$[2a], $[(1)\cdot Fe(CO)_3]$[2b], and $[(1)\cdot Ni(CO)_2]$[1] in which boron metal interactions are present. We now report the first *closo* thiadiborolenebis(metal) compound having a pentagonal bipyramidal structure.

Reaction of *(1)* with $Mn_2(CO)_{10}$ leads to formation of the orange-red complex *(2)* which is thermostable and not air-sensitive but decomposes slowly in chloroform. The mass spectrum (70 eV) of *(2)* contains in addition to the molecular ion $LMn_2(CO)_6^+$ $L=(1)$ ($I_{rel}=6$) the fragments $LMn_2(CO)_4^+$ (21), $LMn_2(CO)_3^+$ (74), $LMn_2(CO)^+$ (36), LMn_2^+ (100), LMn^+ (12), Mn_2S^+ (10), Mn_2^+ (14), Mn^+ (62), and CO^+ (17). The three IR absorptions in the region of the CO stretching vibration and the magnetic equivalence of the methylene protons (Table 1) are in accord with the postulated structure *(2)*



(1)



(2)

(C_{2v} symmetry)[2c]. The upfield shift of $\Delta\delta=43.5$ ppm observed in the ^{11}B-NMR spectrum is indicative of favorable shielding of the boron by increased coordination number compared to the *nido* compounds.

Table 1. Spectroscopic data of *(1)* and *(2)*.

Signal	*(1)*	*(2)*	
^1H-NMR, δ [ppm] against TMS (in $CDCl_3$)			
B—CH_3	0.99 (s, 6)	1.42 (s, 6)	1.36 [a]
C—CH_3	0.87 (t, 6) [b]	1.34 (t, 6) [b]	1.33 [a]
C—CH_2	2.30 (q, 4)	2.52 (q, 4)	2.46 [a]
^{11}B-NMR, δ [ppm] against $BF_3\cdot OEt_2$ (in $CDCl_3$)	66.0 (s)	22.5 (s)	
IR, ν(CO) [cm^{-1}] (in C_2Cl_4)	2021 (s), 1966 (s), 1956 (s)		

[a] In CS_2. [b] $J=7.6$ (±0.1) Hz.

The diamagnetism of *(2)* can be explained under the assumption that the unpaired electrons of the d^7-$Mn(CO)_3$ fragments transfer to the C_2B_2S ring with formation of the $C_2B_2S^{2-}$ dianion isoelectronic with thiophene. As in borolenebis(tricarbonylmanganese) prepared by *Herberich et al.*[3], both $(OC)_3Mn^+$ groups are bound to the ring by six electrons. Hence the structure and bonding of *(2)* also conform to those of a triple-decker complex[3, 4]. According to the $(n+1)$

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electron pair rule[5] for *closo* compounds (n = number of skeletal atoms) 16 skeletal electrons are required for occupation of the bonding molecular orbitals in the 7-atom $Mn_2C_2B_2S$ cluster; these are provided by the components C (2 × 3), B (2 × 2), S (4) and $MnCO_3$ (2 × 1).

3,4-Diethyl-2,5-dimethyl-1,2,5-thiadiborolenebis(tricarbonylmanganese) (2)

A mixture of $Mn_2(CO)_{10}$ (2.67 mmol) and *(1)* (2.67 mmol) in 40 ml mesitylene is heated under reflux for 5 h. The small amount of red $[(1)\cdot Mn(CO)_4]_2$ which crystallizes out on cooling is separated off. After removal of mesitylene by distillation the residue is recrystallized twice from pentane (−20 °C): orange-red crystals, m. p. 183–184 °C, dec. > 230 °C, yield 21 %.

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revised: March 22, 1976
German version: Angew. Chem. *88*, 451 (1976)

CAS Registry numbers:
(1), 54677-51-9; *(2)*, 59318-06-8; $Mn_2(CO)_{10}$, 10170-69-1; ^{11}B, 14798-13-1

[1] Diborylethylene Compounds as Ligands in Metal Complexes, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 3: *W. Siebert, R. Full, C. Krüger,* and *Y.-H. Tsay*, Z. Naturforsch. *31b*, 203 (1976).

[2] a) *K. Kinberger* and *W. Siebert*, unpublished; b) *W. Siebert, G. Augustin, R. Full, C. Krüger,* and *Y.-H. Tsay*, Angew. Chem. *87*, 286 (1975); Angew. Chem. Int. Ed. Engl. *14*, 262 (1975); c) note added in proof (30. 6. 76): confirmed by X-ray structure analysis: *C. Krüger* and *J. Sekutowsky*, unpublished.

[3] *G. E. Herberich*, Lecture at Marburg, January 19, 1976; *G. E. Herberich, J. Hengesbach, U. Kölle, G. Huttner,* and *A. Frank*, Angew. Chem. *88*, 450 (1976); Angew. Chem. Int. Ed. Engl. *15*, 433 (1976).

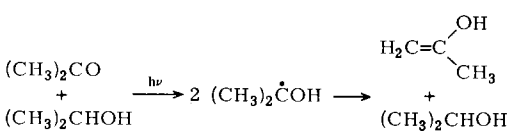
[4] *H. Werner*, Nachr. Chem. Tech. *22*, 3 (1974); *W. T. Robinson* and *R. N. Grimes*, Inorg. Chem. *14*, 3056 (1975); literature cited therein.

[5] *K. Wade*, Chem. Brit. *11*, 177 (1975); literature cited therein.

Enols from Norrish Type II Cleavage of Carbonyl Compounds in Solution

By *Andreas Henne* and *Hanns Fischer*[*]

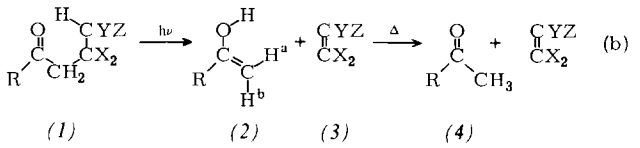
We recently reported that 0.01—0.1 M stationary concentrations of acetone enol are observed during UV irradiation of acetone/2-propanol mixtures at −70 °C, the enol being formed by disproportionation [eq. (a)] of 1-hydroxy-1-methylethyl radicals. It did not decay appreciably within 5000 s[1].



(a)

In this paper, we show that the enols *(2a)*—*(2d)* can be obtained in even higher concentrations from Norrish Type II photoreactions[2] [eq. (b)] of the carbonyl compounds *(1a)*—*(1d)* in appropriate solvents at $T \leq -40$ °C. Only the keto tautomers have previously been reported as products from *(1)* in solution[3].

After 50 minutes' irradiation (filtered light from a Philips SP 1000 W lamp[5], $280 \leq \lambda \leq 350$ nm) of 1 M 5-methyl-2-hexanone *(1a)* in TMS at −70 °C in the sample tube of a VARIAN HA-100 ^{1}H-NMR spectrometer, an NMR spectrum is observed which apart from unconverted reactant *(1a)* (0.13 M), reveals the presence of isobutene *(3a)* (0.80 M), acetone *(4a)* (0.07 M), and acetone enol *(2a)* (0.70 M; NMR[6]: CH_3, $\delta = 1.75$; H^a, $\delta = 3.97$; H^b, $\delta = 3.71$; OH, $\delta = 8.40$ ppm). The concentration of *(2a)* remains approximately constant on



(b)

(1) *(2)* *(3)* *(4)*

	R	X	Y	Z
a	CH_3	H	CH_3	CH_3
b	H	H	H	CH_3
c [4]	$CH_2C(CH_3)_3$	CH_3	H	H
d	C_6H_5	H	H	CH_3

further irradiation, and does not decrease by more than 10 % within 2 h after cessation of irradiation. After briefly warming up the solution to +20 °C a second NMR spectrum is recorded at −70 °C. Evidently an equivalent concentration of *(4a)* has been formed from *(2a)* at +20 °C. Photolysis of *(1a)* in CD_3OD (−70 °C) and CD_3CN/TMS (9:1, −40 °C) produces similar enol concentrations. In the irradiation of *(1b)*—*(1d)* at $T \leq -40$ °C, polar solvents favor[2] the formation of the enols *(2b)*—*(2d)* in high concentrations (Table 1). Warming these enol solutions to room temperature gives the corresponding tautomers *(4b)*—*(4d)*.

The enol-keto tautomerization *(2a)*→*(4a)* was followed between −14 and −35 °C by integration of the NMR signal of the enol at $\delta = 3.97$ ppm (H^1). In TMS, CD_3OH, and CD_3OD this reaction obeys a first order rate law. In TMS the exponential lifetimes of *(2a)* amount to 5300 (−35 °C), 1600 (−26 °C), 560 (−17 °C), and 380 s (−14 °C). For $T \geq -17$ °C these values are smaller than those of di- and trialkyl-substituted enols in solution at 10—37 °C[7]. We believe that the observed lifetimes are determined by acid- or base catalysis arising from solvent impurities or by-products of UV irradiation.

Table 1. Enol concentrations $[(2)]_t$ of *(2a)*—*(2d)* and reactant conversion $[(1)]_0 - [(1)]_t$ (both in mol/l, ±15 %) after irradiation time t at temperature T, starting from *(1a)*—*(1d)* in 1 M solutions.

	T [°C]	t [min]	$[(1)]_0 - [(1)]_t$	$[(2)]_t$
(2a)	−70	50	0.83	0.70 [a]
(2b)	−40	30	0.75	0.20 [b]
(2c)	−40	55	0.72	0.29 [b]
(2d)	−44	30	0.30	0.20 [b]

[a] TMS solvent.
[b] CD_3CN/TMS (9:1) solvent.

In addition to providing a direct proof for the mechanism of the Norrish Type II reactions of *(1a)*—*(1d)* in solution, this observation of enols *(2a)*—*(2d)* in high concentrations may form the basis for the study of enol-keto tautomerizations.

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CAS Registry numbers:
(1a), 110-12-3; *(1b)*, 110-62-3; *(1c)*, 4436-99-1; *(1d)*, 1009-14-9; *(2a)*, 29456-04-0; *(2b)*, 557-75-5; *(2c)*, 59138-75-9; *(2d)*, 4383-15-7; *(4a)*, 67-64-1; *(4b)*, 75-07-0; *(4c)*, 590-50-1; *(4d)*, 98-86-2

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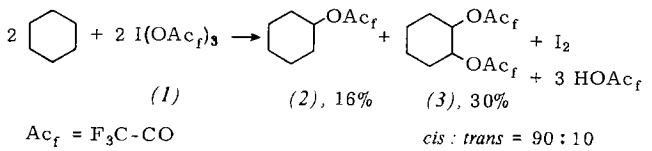
Selective Oxidation of Alkanes and Ethers with Iodine Tris(trifluoroacetate)[**]

By *Joachim Buddrus* and *Horst Plettenberg*[*]

Iodine tris(trifluoroacetate) *(1)* oxidizes numerous organic compounds. After the oxidation of alkenes[1] we now report that of alkanes and ethers.



(1) *(2)*, 16% *(3)*, 30%

$Ac_f = F_3C\text{-}CO$ *cis* : *trans* = 90 : 10

Table 1. Oxidation of alkanes and ethers with iodotris(trifluoroacetate) *(1)* at room temperature.

Alkane or ether	Time, solvent	Products [a] and yields [b]
$H_3C\text{-}CH_2\text{-}CH_2\text{-}CH_3$ *(7)*	14 d, without solvent	$H_3C\text{-}CH(OAc_f)\text{-}CH_2\text{-}CH_3$ *(8)*, 11%; $H_3C\text{-}CH(OAc_f)\text{-}CH(OAc_f)\text{-}CH_3$ *(9)*, 26%, *meso*:*racem* = 44 : 56; $H_3C\text{-}C(CH_2\text{-}CH_3)(OAc_f)_2$ *(10)*, 3%
$H_3C\text{-}CH(CH_3)\text{-}CH_3$ *(11)*	1 h, CH_2Cl_2	$H_3C\text{-}C(CH_3)(OAc_f)\text{-}CH_3$ *(12)*, < 1%; $H_3C\text{-}C(CH_2)(OAc_f)_2$ *(13)*, 60%
Norbornane	2d, CH_2Cl_2	2-Norbornyl trifluoroacetate 68%, *exo*:*endo* = 99.9:0.1
(14)	10 min, pentane	*(15)*, 73%
Adamantane	30 min, pentane	1-Adamantyl trifluoroacetate 95%
(16)	10 min, pentane	*(17)*, 64%, *cis*:*trans* = 12 : 88
(18)	10 min, pentane	$CH(OAc_f)_2$ *(19)*, 14%; *(20)*, 42%, *cis* : *trans* = 50 : 50
$CH_2\text{-}OAc_f$ *(21)*	10 min, pentane	*(22)*, 55%, *r*-2, *t*-3, *t*-5; *r*-2, *t*-3, *c*-5; *r*-2, *c*-3, *t*-5; *r*-2, *c*-3, *c*-5 = 32 : 49 : 11 : 8

[a] Structures in accord with 1H-NMR spectra.
[b] Yields determined partly by weighing (for homogeneous fractions) partly by quantitative gas chromatography utilizing an authentic sample (for mixed fractions) and refer to *(1)* and its reduction to iodine.

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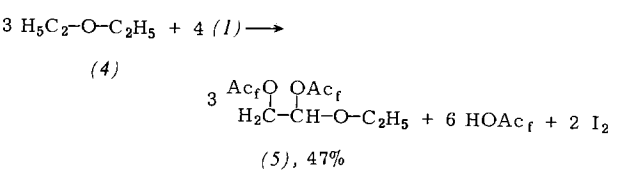
If *(1)* is suspended at room temperature in an alkane (or dissolved together with the alkane in a solvent such as dichloromethane), then the alkane is oxidized mainly to mono- and bis(trifluoroacetoxy) derivatives of types *(2)* and *(3)*, while *(1)* is converted into iodine.

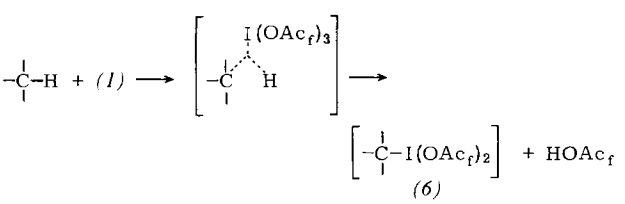
Alkanes having tertiary CH groups are oxidized within minutes, those with secondary CH_2 groups within days, and alkanes of neopentane type not at all (Table 1). Reaction of *(1)* with ethers is even faster, involving selective α,β-oxidation with formation of α,β-bis(trifluoroacetoxy) derivatives of type *(5)*. With lead tetraacetate α,β-oxidation occurs only with secondary ethers[2].



(5), 47%

The rate of oxidation of alkanes (and other compounds) increases with increasing electronegativity of the substituent attached to iodine, as shown for instance by experiments with cyclohexane: iodine triacetate[3] does not react at all with it, iodine tris(trifluoroacetate) *(1)* in about three days, and iodine tris(trifluoromethansulfonate)[4] immediately.

The reactions are presumably initiated by an electrophilic attack on the C—H bond, whose σ basicity has been repeatedly demonstrated[5]. Whether the attacking species is *(1)*, $I(OAc_f)_2^{\oplus}$, or even $IOAc_f$ has not been established. Derivatives of (dihydroxyiodo)alkanes, *e.g. (6)*, are unstable (unless the alkyl group is perfluorinated[6]) and undergo 1,1-elimination to give alkyl trifluoroacetates, *e.g. (2)*, or 1,2-elimination affording an alkene which is oxidized stereoselectively to alkylene bis(trifluoroacetates), *e.g. (3)*[1]. The observation that 2-iodobutane gives the same products as butane on treatment with *(1)* suggests that the reaction proceeds *via* bis(trifluoroacetoxy)iodoalkanes *(6)*.



(6)

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CAS Registry numbers:
(1), 14353-86-7; *(2)*, 1549-45-7; *cis-(3)*, 41049-51-8; *trans-(3)*, 27088-69-3; *(4)*, 60-29-7; *(5)*, 59368-01-3; *(7)*, 106-97-8; *(8)*, 1536-78-3; *meso-(9)*, 41049-49-4; *racemic-(9)*, 41049-50-7; *(10)*, 59368-02-4; *(11)*, 75-28-5; *(12)*, 400-52-2; *(13)*, 41049-48-3; *(14)*, 2825-83-4; *(15)*, 59368-03-5; *(16)*, 110-00-9; *cis-(17)*, 59368-04-6; *trans-(17)*, 59368-05-7; *(18)*, 142-68-7; *(19)*, 59368-06-8; *cis-(20)*, 59368-07-9; *trans-(20)*, 59368-08-0; norbornane, 279-32-2; *exo*-2-norbornyl trifluoroacetate, 31024-13-2; *endo*-2-norbornyl trifluoroacetate, 31076-61-6; adamantane, 281-23-2; 1-adamantyl trifluoroacetate, 58652-54-3

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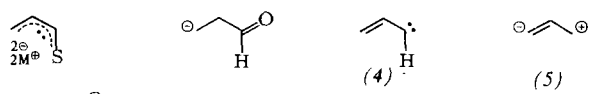
The Magnesium Derivative of Thioacrolein Dianion. A Facile Entry to Vinyl- and Divinyloxiranes[**][1]

By *Dieter Seebach*, *Karl-Heinz Geiss*, and *Manat Pohmakotr*[*]

We recently succeeded in preparing[2, 3] the dianions of the thiocarbonyl compounds thiobenzaldehyde and thioacrolein, which as neutral molecules can exist only at extremely low temperatures[4], in the form of their dilithium derivatives by direct abstraction of two protons from benzyl and allyl thioalcohol, respectively. The organolithium compound *(1)* reacts with electrophiles preferentially in the γ-position to the hetero atom and is thus synthetically equivalent to the anion *(3)*[3, 5]. We now wish to describe the reactions of

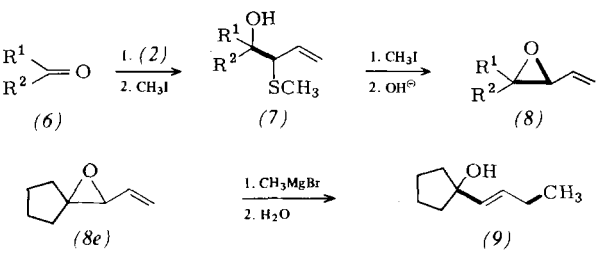


(1), 2 $M^{\oplus}$ = 2 $Li^{\oplus}$ *(3)* *(4)* *(5)*

(2), 2 $M^{\oplus}$ = $Mg^{2\oplus}$

the magnesium derivative *(2)*, readily accessible from *(1)* by transmetalation (addition of 1 equiv. of $MgBr_2$), with aldehydes and ketones which occur almost exclusively (>90 %) in the α-position to the sulfur atom and confer upon this reagent the properties of a synthetic building block with reactivities as shown in *(4)* and *(5)*.

Successive addition of a saturated or α,β-unsaturated aldehyde or ketone *(6)* and methyl iodide to a solution of *(2)* at −80 °C affords very high yields of the adducts *(7)*. Methylation to give the sulfonium salt—again with CH_3I (1.0—1.5 equiv., pure)—and base-induced elimination (0.5 N NaOH/CH_2Cl_2)[6a] converts *(7)* into the vinyloxiranes *(8)* (examples given in Table 1).



(6) *(7)* *(8)* *(8e)* *(9)*

Vinyloxiranes *(8)* are thus accessible more easily and in higher yields than *via* sulfur ylides[6b]. Divinyloxiranes of type *(8c)* and *(8g)* (3,4-epoxides of 1,3,5-hexatrienes) cannot be prepared by C—C linkage *via* the ylides since the latter cyclopropanate α,β-unsaturated carbonyl compounds[6b]. The epoxides *(8)* are useful highly reactive intermediates for the preparation of other compounds. For instance, the three-membered ring in *(8e)* is opened by methylmagnesium bromide to form *(9)*[7] [see *(5)*]; vinyloxiranes undergo thermal rearrangement to dihydrofurans[8a], and divinyloxiranes to 4,5-dihydrooxepins[8b].

Finally, we have also been able to demonstrate in the case of the adduct of *(2)* to methyl vinyl ketone *(6g)* that the 1,2-α-reaction can be transformed into a 1,4-γ-reaction: the potassium alkoxide *(10)* of the product *(7g)* undergoes a Cope rearrangement[9] forming the thioenol ether *(11)* of

Table 1. Synthesis of vinyloxiranes *(8)* *via* the β-(methylthio)alcohols *(7)*. Aldehydes and unsymmetrical ketones *(6)* give mixtures of diastereomers.—Elemental analyses within 0.4 % of the theoretical values are available for products *(7)* and *(8)* listed; IR and NMR spectral data are compatible with the structures.

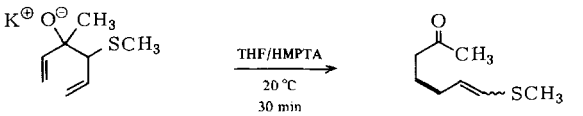
	R^1	R^2	*(7)* [a] Yield [%]	*(8)* Yield [%] after distillation	B.p [b] [°C/torr]
a	C_2H_5	H	91	48	70/130
b	$CH(CH_3)_2$	H	98	63	60/18
c	CH=CH—CH_3	H	95	47	80/20
d	C_6H_5	H	73	—	—
e [c]	—$(CH_2)_4$—		94	78	70/22
f	C_6H_5	CH_3	89	70	100/15
g [d]	$CH=CH_2$	CH_3	84	52	80/20
h	$(CH_3)_2C=CH$	CH_3	95	—	—
i	—CH=CH—$(CH_2)_2$—		90	—	—
j	—CH=CH—$(CH_2)_3$—		91	75	70/0.5

[a] Determined by NMR spectroscopy; the yields of distilled analytically pure products are 10—20 % lower. The crude products *(7)* can be converted directly into *(8)*.

[b] Oil bath temperature on molecular distillation.

[c] With 1 equiv. of CH_3MgBr in ether (−80 to 0 °C) compound *(8e)* affords the alcohol *(9)* (70 % yield, 95 % pure according to GC, b.p. 80—90 °C/2 torr [b]).

[d] With KH in THF/HMPA *(7g)* reacts *via* the alkoxide *(10)* to give the ketone *(11)* (63 % yield after distillation; b.p. 80 °C/0.4 torr [b]).



(10) *(11)*

1,2-adduct with *(6g)*, α-adduct with *(2)*

1,4-adduct with *(6g)*, γ-adduct with *(2)*

a 1,6-dicarbonyl derivative. All the C—C bonds newly linked with the aid of *(2)* as synthon are shown in bold print.

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CAS Registry numbers:
(2), 59231-09-3; *(6a)*, 123-38-6; *(6b)*, 78-84-2; *(6c)*, 4170-30-3; *(6d)*, 100-52-7; *(6e)*, 120-92-3; *(6f)*, 98-86-2; *(6g)*, 78-94-4; *(6h)*, 141-79-7; *(6i)*, 930-30-3; *(6j)*, 930-68-7; *(7a)*, 53634-97-2; *(7b)*, 59231-10-6; *(7c)*, 59231-11-7; *(7d)*, 53693-81-5; *(7e)*, 53634-98-3; *(7f)*, 53634-99-4; *(7g)*, 59231-12-8; *(7h)*, 59231-13-9; *(7i)*, 59231-14-0; *(7j)*, 59231-15-1; *(8a)*, 34485-78-4; *(8b)*, 59231-16-2; *(8c)*, 59270-11-0; *(8e)*, 59231-17-3; *(8f)*, 59231-18-4; *(8g)*, 59231-19-5; *(8j)*, 59231-20-8; *(9)*, 59231-21-9; *(10)*, 59231-22-0; *(11)*, 59231-23-1

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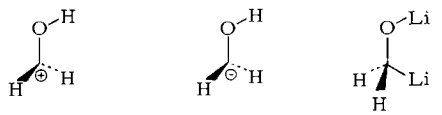
[7] Cf. *G. C. M. Aithie* and *J. A. Miller*, Tetrahedron Lett. *1975*, 4419, references cited therein.
[8] a) *J. C. Paladini* and *J. Chuche*, Bull. Soc. Chim. Fr. *1974*, 197; b) *J. C. Pommelet*, *N. Manisse*, and *J. Chuche*, Tetrahedron *28*, 3929 (1972).
[9] Cf. *R. E. Ireland* and *R. H. Mueller*, J. Am. Chem. Soc. *94*, 5897 (1972); *D. A. Evans* and *A. M. Golob*, *ibid.* *97*, 4765 (1975).

Doubly Metalated Methanol—A Nucleophilic Hydroxymethylation Reagent[**]

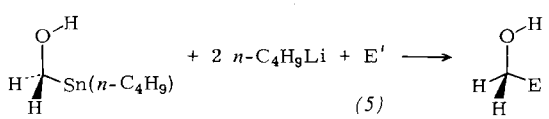
By *Dieter Seebach* and *Norbert Meyer*[*]

Protonated formaldehyde *(1)* is available as an electrophilic hydroxymethylation reagent for synthetic operations[1]. An umpolung of the normal reactivity of *(1)* would be present in *(2)*, which being a tautomer of the methoxide ion is of course not accessible as such.



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

We have found that the alcohol *(4)* available from $(n\text{-}C_4H_9)_3SnMgCl$ and monomeric formaldehyde[2] affords products of type *(6)* on successive addition of *two* equivalents of *n*-butyllithium and one equivalent of an electrophile *(5)* (see experimental procedure and Table 1). Compound *(4)* is probably converted by deprotonation *and* tin/lithium exchange[3] into the dilithium derivative[4] *(3)* which is attacked by electrophiles at the C atom. *(3)* can be regarded as the Li_2 derivative of doubly deprotonated methanol[5]. The reactions leading to *(6c)* to *(6e)* described in this communication are the first direct hydroxymethylations[6] of carbonyl compounds.



(4) *(5)* *(6)*

Table 1. Hydroxymethylation products *(6)* of alkyl halides and carbonyl compounds. Compounds *(6)* are already known. All the physical and spectroscopic data of the samples we isolated accord with those reported in the literature.

	Electrophile E' *(5)*		E	Products *(6)* Yield [%]	Physical data
a	*n*-Octyl chloride	*a*	$n\text{-}C_8H_{17}$	53	$n_D^{20}=1.4335$
b	*n*-Octyl bromide	*a*	$n\text{-}C_8H_{17}$	45	$n_D^{20}=1.4330$
c	Benzyl bromide	*b*	$C_6H_5—CH_2$	45	$n_D^{19}=1.5260$
d	Benzaldehyde	*c*	$C_6H_5—CH(OH)$	62	m.p. 66.0 °C
e	Cyclohexanone	*d*	$(CH_2)_5C(OH)$	46	m.p. 77.1 °C
f	Di-*tert*-butyl ketone	*e*	$[(CH_3)_3C]_2C(OH)$	41	$n_D^{20}=1.4705$

α-Phenylglycol (6c)

A 1.6 N solution of *n*-butyllithium in hexane (12.5 ml, 20 mmol) is added under argon to a stirred solution of *(4)* (3.2 g, 10 mmol) in light petroleum (b.p. 30—40 °C) at −20 °C. After removal of the bath and 6 hours' stirring at room temperature, the homogeneous solution is cooled to −78 °C and treated with benzaldehyde *(5d)* (1.06 g, 10 mmol). A colorless precipitate is formed. The mixture is allowed to warm up overnight, poured into saturated brine, the phases separated, the aqueous phase extracted with ether, and the combined organic phases dried over K_2CO_3. The residue obtained on evaporation is partly crystalline. Digestion with pentane, cooling to 0 °C, and filtration affords 0.85 g (6.2 mmol) of *(6c)*.

The other products *(6)* listed in Table 1 were prepared in similar manner. Tetrabutyltin can be isolated in 90 % yield in all cases. It can be separated from liquid products *(6)* by filtration of a pentane solution over silica gel.

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[**] Part of projected thesis of *N. Meyer*, Universität Giessen. *N. M.* thanks the Studienstiftung des Deutschen Volkes for a grant.—This work was supported by the Fonds der Chemischen Industrie. We are grateful to the Schering company, Bergkamen, for a gift of tributyltin chloride.

[1] See, *e.g.*, the Prins reaction: *J. Mathieu* and *J. Weill-Raynal*: Formation of C—C Bonds. Thieme, Stuttgart 1973, Vol. 1, references cited on pp. 18—33.
[2] *J. C. Lahournère* and *J. Valade*, C. R. Acad. Sci. *C 270*, 2080 (1970).
[3] It is already known that alkoxymethyllithium (*U. Schöllkopf* in Houben-Weyl-Müller: Methoden der Organischen Chemie. Thieme, Stuttgart 1970, Vol. 13/1, p. 133) and dialkylaminomethyllithium compounds [*D. J. Peterson* and *J. F. Ward*, J. Organomet. Chem. *66*, 209 (1974), references cited therein] can be prepared by Sn/Li exchange.
[4] Cf. also doubly metalated thiols: *D. Seebach* and *K. H. Geiss*, Angew. Chem. *86*, 202 (1974); Angew. Chem. Int. Ed. Engl. *13*, 202 (1974); *K. H. Geiss, B. Seuring, R. Pieter*, and *D. Seebach, ibid. 86*, 484 (1974) and *13*, 479 (1974), respectively; *D. Seebach, K. H. Geiss*, and *M. Pohmakotr, ibid. 88*, 449 (1976) and *15*, 437 (1976), respectively.
[5] According to *D. O. DePree* and *J. D. Johnston*, US-Pat. 3239568; Chem. Abstr. *64*, 15921e (1966), double metalations are feasible under extreme conditions. We were unable to obtain a reagent of type *(3)* by reaction of formaldehyde with alkali metals. The high solubility of our reagent in pentane, even at −78 °C, indicates that *(3)* is somehow "complexed" with the R_4Sn present in the solution!
[6] Hydroxymethylation of an alkyl halide has been performed with $LiCH_2BR_2$ [*M. W. Rathke* and *R. Kow*, J. Am. Chem. Soc. *94*, 6854 (1972)].

Synthesis of the γ-Octose of the Quinocycline Complex[**]

By *Hans Paulsen* and *Volker Sinnwell*[*]

The anthracycline antibiotics of the quinocycline complexes isolated from *Streptomyces aureofaciens* contain a hydroxyethyl-branched octose as carbohydrate component[2, 3]. We have synthesized the γ-octose occurring in quinocycline A and isoquinocycline A. In order to elucidate the remarkable stereochemistry of the reaction sequences and their products, the experiments were first performed with the economically accessible compounds of the D series.

Reaction of the epoxy ketose *(6)* with 2-lithio-1,3-dithiane unexpectedly affords *(1)* and *(2)*. The desired adduct having the 4-OH group *trans* to the epoxy group was not observed since it undergoes quantitative epoxide rearrangement[1] into *(1)*. Epoxide rearrangement can be largely suppressed by use of a less polar carbanion. Thus treatment of *(6)* with vinyllithium affords not only *(11)* but also the desired product *(7)* which undergoes only slight rearrangement (10 %).

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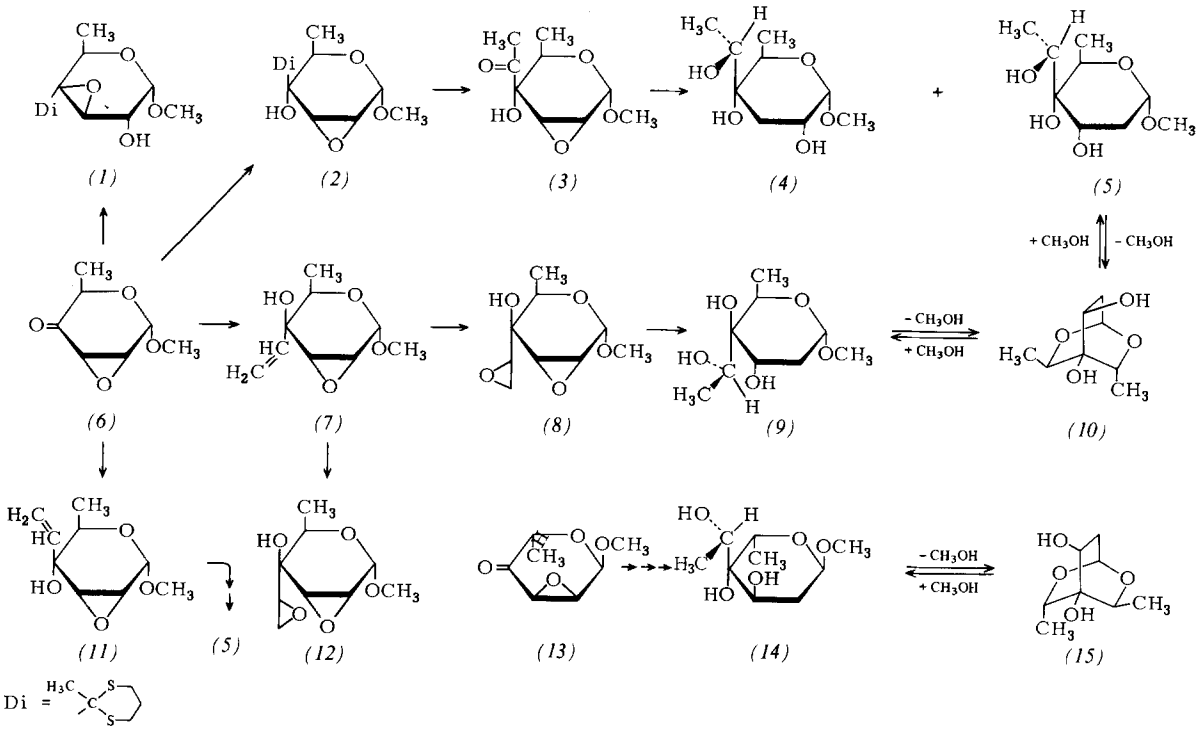
[**] Branched-Chain Sugars, Part 13.—Part 12: ref. [1].

Epoxidation of *(7)* with *m*-chloroperbenzoic acid yields the separable diepoxides *(8)* and *(12)* which can both be selectively reduced with $LiAlH_4$. On reaction of *(8)* with $LiAlH_4$ the epoxide rings are selectively opened at C-2 and C-8. The resulting octose *(9)* (syrup; $[\alpha]=+109.4°$) is the

CAS Registry numbers:
(3), 59463-78-4; *(4)*, 59463-79-5; *(5)*, 59463-80-8; *(6)*, 55533-59-0; *(7)*, 59463-81-9; *(8)*, 59463-82-0; *(9)*, 59463-83-1; *(10)*, 59463-84-2; *(11)*, 59463-85-3; *(12)*, 59463-86-4; *(13)*, 59463-87-5; *(15)*, 59492-29-4; 2-lithio-1,3-dithiane, 36049-90-8; *m*-chloroperbenzoic acid, 937-14-4



D-form of the natural product. Acidic glycosidic cleavage converts *(9)* into the well-crystalline anhydro compound *(10)* (m.p. 146°C; $[\alpha]=+146°$)[4]. The isomeric octoses do not form anhydro compounds so readily. The dioxabicyclo[2.2.2]octane system *(10)* is stabilized by the screw-shaped arrangement of the substituents (right-handed screw in this case).

Surprisingly, *(10)* is also accessible from *(5)*, the product with the "wrong" stereochemistry at the branching point. Compound *(5)* is preparable from *(11)*, or better from *(2)*. The desulfuration product *(3)* obtained from *(2)* undergoes selective reaction in the side chain with $LiAlH_4$ but not in the epoxide ring, thus yielding *(4)* and *(5)*. Hydrolysis of *(5)* likewise furnishes *(10)*.

After clarification of all points in the D series, a direct synthesis was performed in the L series. Starting from the L-epoxy ketose *(13)* *via* compounds corresponding to *(7)* and *(8)* we obtained the octose *(14)* (syrup; $[\alpha]=-101.4°$), which is identical with the natural product. Hydrolysis of *(14)* leads to the L-anhydro compound *(15)* (m.p. 146—147.5°C; $[\alpha]=-147.6°$) with a left-hand screw arrangement of substituents.

It is important that acidic methanolysis of *(5)* leads *via* the equilibrium *(5)*⇋*(10)*⇋*(9)* to an isomerization of *(5)* to *(9)* (α,β form); *(9)* is considerably more stable than *(5)*. Accordingly, no information about the stereochemistry at the branching point of the octose is available from hydrolysis of the quinocycline complex. Fortunately, this question is answered by an X-ray structure analysis of isoquinocycline A[5]. Uncertainty surrounded the stereochemistry in the side chain[6], which has now been established by the above series of reactions.

Received: April 26, 1976 [Z 461a IE]
German version: Angew. Chem. *88*, 476 (1976)

[1] *H. Paulsen* and *W. Koebernick*, Tetrahedron Lett., in press.
[2] *W. D. Celmer, K. Murai, K. V. Rao, F. W. Tanner, Jr.*, and *W. S. Marsh*: Antibiotics Annual (1957—58). Medical Encyclopedia, Inc., New York 1959, p. 481.
[3] *U. Matern* and *H. Grisebach*, Eur. J. Biochem. *29*, 1 (1972).
[4] *J. S. Welb, R. W. Broschard, D. B. Cosulich, J. H. Mowat*, and *J. E. Lancaster*, J. Am. Chem. Soc. *84*, 3183 (1962).
[5] *A. Tulinsky*, J. Am. Chem. Soc. *86*, 5369 (1964).
[6] *A. Tulinsky*, East Lansing, Michigan (USA), personal communication.

C—C Linkage of Polyfunctional Molecules by Nucleophilic Addition of Dianions. Synthesis of Pillarose[**]

By *Hans Paulsen, Klaus Roden, Volker Sinnwell*, and *Wolfgang Koebernick*[*]

The scope of nucleophilic addition for forming C—C linkages[2, 3] is drastically restricted if the potential carbanion bears an oxygen atom bound to the α position as an ether, ester, or acetal. On metalation of such compounds, *e.g.* 1,3-dithiane derivatives, direct elimination of RO ensues to form olefins and decomposition products.

The problem can be solved by reacting the free alcohols with the metalating reagent in the molar ratio 1:2, thus converting them into dianions. 2-(1,3-Dithiane)methanol reacts with *n*-butyllithium in THF at −70°C to give the dianion *(2)* which is sufficiently stable under the reaction conditions and reacts almost as well as the 1,3-dithiane monoanion with carbonyl groups. We selected the *galacto*-6-aldehyde *(1)* as

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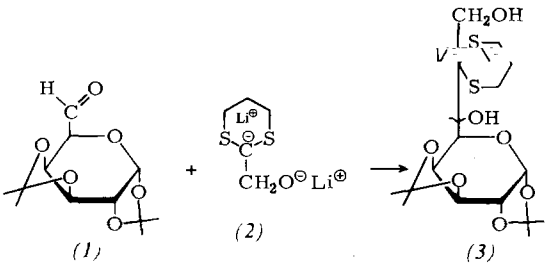
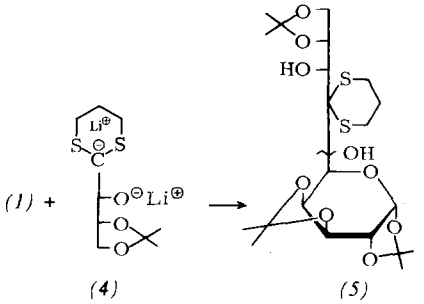
[**] Branched-Chain Sugars, Part 14.—Part 13: ref. [1].

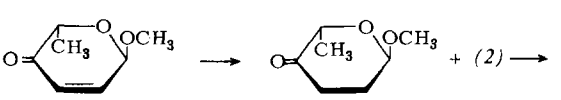
test substance, which smoothly reacts with *(2)* to form the functionalized two-membered chain, thus giving a 54 % yield of *(3)*.



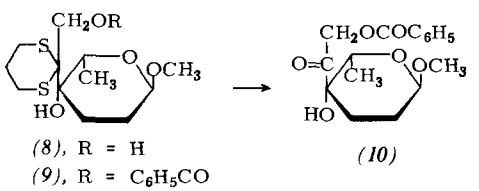
(1) *(2)* *(3)*



(4) *(5)*



(6) *(7)*



(8), R = H
(9), R = C_6H_5CO *(10)*

In order to establish whether the functionalized chain on the 1,3-dithiane group can be elongated, the trimethylene dithioacetal of 3,4-*O*-isopropylidene-D-erythrose was prepared and reacted with *n*-butyllithium in the molar ratio 1:2 at −70 °C in THF. The labile dianion *(4)* that was formed was also reacted with the aldehyde *(1)*. The long-chain sugar *(5)* having ten C atoms is obtained. The process appears to have scope for extension and to be suitable for linkage of prefabricated polyfunctional structural units.

Application of the new process will now be illustrated by the synthesis of the branched-chain sugar pillarose which thus becomes accessible in just a few steps. Pillarose is the carbohydrate component of the antibiotic pillaromycin A isolated from *Streptomyces flavovirens*, which possesses a tetracyclic aglycon and belongs to the group of the anthracyclines which exhibit antitumor activity[4].

The ketose *(7)* obtained from the enone *(6)*[5] by selective hydrogenation shows a strong preference to form *(8)* on reaction with the dianion *(2)*. The two isomeric branched-chain sugars expected as products are formed in the ratio of 9:1. The isomer *(8)* can be crystallized directly (45 %; m.p. 125—127 °C; $[\alpha]_D^{20} = -108°$); its selective benzoylation affords *(9)* (87 %; m.p. 123—124 °C, $[\alpha]_D^{20} = -81.1°$). Desulfuration with $HgO/BF_3 \cdot Et_2O$ furnishes the pillaroside *(10)* (60 %; m.p. 104—106 °C, $[\alpha]_D^{20} = -96°$). The monobenzoate *(10)* is the best-described derivative of pillarose. The physical data and the NMR spectrum are in accord with those of the natural product.

The structure of pillarose[4] has only recently been established by *Fraser-Reid*[6]. The compound *(10)* synthesized corresponds to the relevant formula.

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CAS Registry numbers:
(1), 4933-77-1; *(2)*, 59464-28-7; *(3)*, 59464-29-8; *(4)*, 59464-30-1; *(5)*, 59464-31-2; *(6)*, 55102-46-0; *(7)*, 59492-30-7; *(8)*, 59464-32-3; *(9)*, 59464-33-4; *(10)*, 59531-21-4; 2-(1,3-dithiane)methanol, 37721-88-3

[1] *H. Paulsen* and *V. Sinnwell*, Angew. Chem. *88*, 476 (1976); Angew. Chem. Int. Ed. Engl. *15*, 438 (1976).
[2] *D. Seebach*, Synthesis *1969*, 17.
[3] *H. Paulsen*, *V. Sinnwell*, and *P. Stadler*, Chem. Ber. *105*, 1978 (1972).
[4] *M. Asai*, *E. Mizuta*, *A. Mikaye*, and *S. Tatsuoka*, Chem. Pharm. Bull. *18*, 1699, 1706, 1713, 1720 (1970).
[5] *H. Paulsen* and *W. Koebernick*, Tetrahedron Lett., in press.
[6] *J. O. Pezzanite*, *J. Clardy*, *P.-Y. Lau*, *G. Wood*, *D. L. Walker*, and *B. Fraser-Reid*, J. Am. Chem. Soc. 97, 6250 (1975); *D. L. Walker* and *B. Fraser-Reid*, *ibid.* *97*, 6253 (1975).

Synthesis of α-Glycosidically Linked Disaccharides of D-Galactosamine[**]

By *Hans Paulsen*, *Čeněk Kolář*, and *Wolfgang Stenzel*[*]

The determinant group of the blood-group specific glycoproteins of type A contains α-glycosidically linked D-galactosamine as the most important component[2, 3]. The same structural unit also occurs in several glycoproteins[3]. A selective synthesis of α-glycosides of D-galactosamine has hitherto been precluded by the inaccessibility of suitable starting compounds and the difficulties involved in application of the "nitrosoglycal method"[4]. We have now been able to solve this problem by use of the "azide method"[5].

The *talo*-epoxide *(1a)* readily available from 1,6-anhydro-β-D-galactose reacts with NaN_3 in ethanol/water to give the 2-azidogalacto compound *(2a)* (74 %; m.p. 89 °C; $[\alpha]_D^{20} = +20.0°$). After benzylation to give *(2b)*, acetolysis to form *(3)* (89 %; syrup; $[\alpha]_D^{20} = +53.0°$) becomes possible. Compound *(3)* can be converted into the α-bromide *(4)* (87 %; syrup; $[\alpha]_D^{20} = +141.0°$) at −20 °C in dichloromethane/HBr. β-Glycosides can be prepared selectively from *(4)*. Thus *(4)* affords the β-glycoside *(8)* (82 %; syrup; $[\alpha]_D^{20} = -39.0°$) on treatment with benzyl alcohol in the presence of Ag_2CO_3/Drierite.

For selective synthesis of α-glycosides compound *(4)* is inverted to the β-chloride *(5)* in a kinetically controlled reaction with tetraethylammonium chloride in acetonitrile. The reaction is monitored by polarimetry and stopped at minimum rotation ($[\alpha]_D^{20} = +30.4°$). The reaction product, which has to be subjected to further reaction immediately upon work-up, affords α-glycosides with alcohols in the presence of Ag_2CO_3.

In order to test the disaccharide synthesis, compound *(5)* was reacted with the 2-azido-*gluco* compound *(6)* in the presence of catalytic amounts of $AgClO_4$. A 66% yield of disaccharide is obtained showing an α,β ratio of 10:1. The α-(1→3)-linked disaccharide *(7)* could be isolated in crystalline form (53 % yield; m.p. 41 °C; $[\alpha]_D^{20} = 98.2°$); the α linkage is confirmed by 270 MHz NMR spectra. The azido glycosides are readily convertible into amino glycosides by hydrogenation

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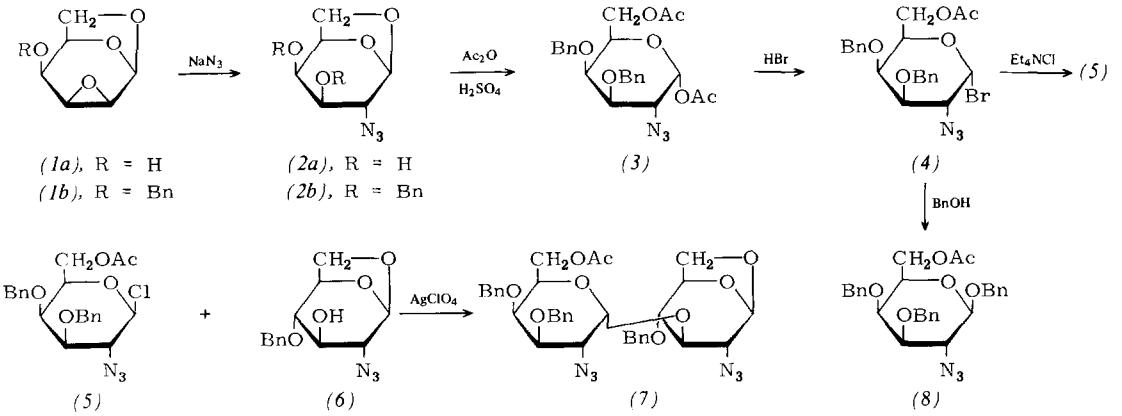
[**] Building Units of Oligosaccharides, Part 3.—Part 2: ref. [1].



according to known methods. Thus a pathway is now available for selective synthesis of α-glycosides of D-galactosamine.

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CAS Registry numbers:
(1a), 6893-59-0; (2a), 59464-21-0; (2b), 59464-22-1; (3), 59464-23-2; (4), 59464-24-3; (5), 59464-25-4; (6), 55682-47-8; (7), 59464-26-5; (8), 59464-27-6; 1,6-anhydro-β-D-galactose, 644-76-8; benzyl alcohol, 100-51-6; tetraethylammonium chloride, 56-34-8

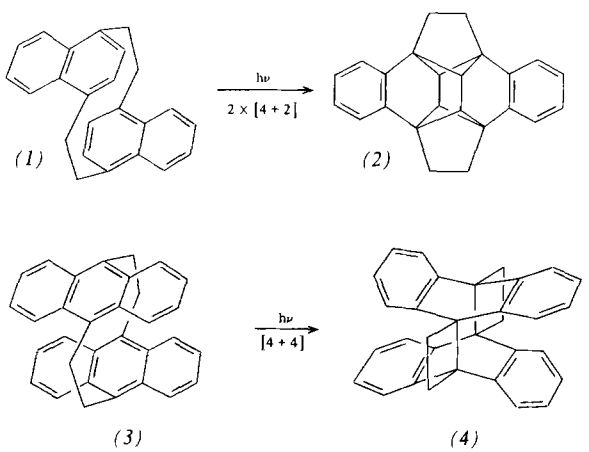
[1] H. Paulsen, O. Lockhoff, B. Schröder, B. Sumfleth, and W. Stenzel, Tetrahedron Lett., in press.
[2] R. Montgomery in W. Pigman and D. Horton: The Carbohydrates. Academic Press, New York 1970, Vol. IIB, p. 689.
[3] A. Gottschalck: Glycoproteins. Elsevier, Amsterdam 1966.
[4] R. U. Lemieux, K. James, and T. L. Nagabushan, Can. J. Chem. 51, 42, 48 (1973).
[5] H. Paulsen and W. Stenzel, Angew. Chem. 87, 547 (1975); Angew. Chem. Int. Ed. Engl. 14, 558 (1975).

Intramolecular [4+4]Photocycloaddition of [2.2](1,4)-Naphthalenophane

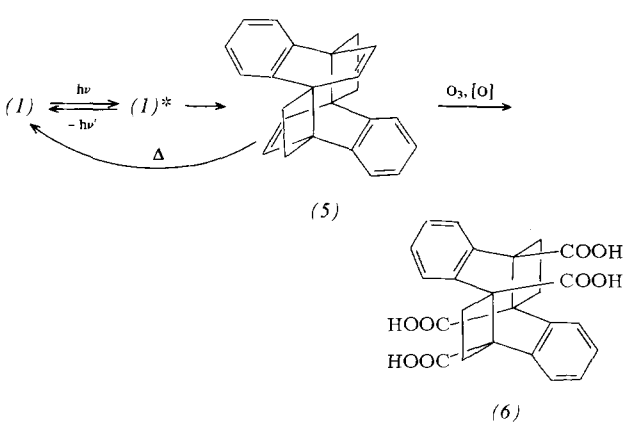
By *Gerd Kaupp* and *Inge Zimmermann*[*]

The twofold intramolecular Diels-Alder reaction occurring on ten days' irradiation of *anti*-[2.2](1,4)naphthalenophane *(1)* to form dibenzoequinene *(2)*[1] is exceptional. The related [2.2](9,10)anthracenophane *(3)* is known to undergo particularly smooth [4+4]photocycloaddition to give *(4)*[2], and numerous naphthalene derivatives suffer intermolecular [4+4]photodimerizations[3]. Since the well-proved approach of empirical conformational analysis with the aid of molecular models[2,4] also suggest the [4+4]reaction to be more favorable geometrically than [4+2]addition in the case of *(1)*, we have examined the photodeactivation of *(1)* by spectroscopic and chemical methods and now report new findings which confirm the predictions of conformational analysis.

Ethano bridges maintain the internal six-membered rings of *(1)* [as in *(3)*][2] in close proximity. Expectedly, a UV spectrum is found [cyclohexane: $\lambda_{max}(\varepsilon)=238$ (39000), 246 (37000), 273 (sh, 6200), 283 (sh, 5600), 302 (sh, 5500), 310 (6000), 320 (sh, 4850), 327 (sh, 3700), 333 nm (sh, 2400)] which extends to higher wavelengths (up to *ca.* 355 nm) than that of 1,4-dimethylnaphthalene[1]. Electronically excited *(1)* must accordingly be regarded, like *(3)*, as an example of an intramolecular excimer. Unlike *(3)*[2], which undergoes exclusive photochemical deactivation, it emits a very broad structureless excimer fluorescence (cyclohexane: $\lambda_{max}^{corr.}=416$ nm; $\Phi_{Fl}=0.021$; acetonitrile: $\lambda_{max}^{corr.}=411$ nm). Even at −196 °C (ether/ethanol = 1:2; $\lambda_{max}^{corr.}=420$ nm) it remains unstructured and is far more intense than the phosphorescence of *(1)* ($\lambda_{max}^{corr.}=527$, 542, 549, 572, 592, 615 nm; $\tau_{Ph}=0.24$ s)[5].



Apart from luminescence, a diminution of the UV absorption with concomitant formation of the [4+4]product *(5)* is observed on long-wave excitation (above 290 nm).



Compound *(5)* is thermolabile. At room temperature it undergoes extremely rapid rearomatization to regenerate *(1)* ($t_{1/2}=76$ s at 20 °C). According to UV analysis this back-reaction is first-order when performed between −15 and +25 °C in toluene and has an activation energy of $E_a=18.65$ kcal/mol

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and a frequency factor $A=10^{11.85}\,s^{-1}$. Thus derivatization must be performed at as low a temperature as possible. In order to prepare *(6)* [m.p. 315°C (dec.)] compound *(1)* (200 mg) is irradiated in toluene for 1 h (Philips HPK 125 W, Pyrex filter), then ozonized at −80°C with addition of methanol and subjected to oxidative work-up[6].

The cyclic process *(1)* ⇌ *(5)* ⇌ *(1)* proceeds highly uniformly so that at temperatures above 20°C and on prolonged irradiation the thermally more stable escape product *(2)* can be formed (25%; 10 d; 16 fluorescent lamps)[1], although there is no conceivable conformer of *(1)* in which [4+2] reactions giving *(2)* would be geometrically favored over the kinetically preferred [4+4] reaction to form *(5)*.

Since the presumably [as for *(3)* $\overset{h\nu}{\rightleftharpoons}$ *(4)*][2] two-step formation of *(5)* must compete with relatively intense excimer luminescence it would appear to be geometrically hindered. Thus it must be assumed that the internal aromatic rings of the conformers of *(1)* which absorb at longer wavelengths are laterally displaced and not completely parallel to each other. In this way excessive steric interactions are avoided between aliphatic and *peri* H atoms, and photoreaction after long-wave excitation can only occur subsequent to a slight conformational change. A thermal activation threshold must be overcome in the process, for the photochemical [4+4] reaction of *(1)* to form *(5)* (313; 334 nm) is no longer observed at −190°C.—Excitation at shorter wavelengths leads to [6+6] cleavage[7].

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German version: Angew. Chem. *88*, 482 (1976)

CAS Registry numbers:
(1), 14724-91-5; *(2)*, 15129-78-9; *(3)*, 5672-97-9; *(5)*, 59473-47-1; *(6)*, 59473-48-2

[1] *H. H. Wasserman* and *P. M. Keehn*, J. Am. Chem. Soc. *91*, 2374 (1969); *89*, 2770 (1967).

[2] *G. Kaupp*, Angew. Chem. *84*, 259 (1972); Angew. Chem. Int. Ed. Engl. *11*, 313 (1972); Justus Liebigs Ann. Chem. *1973*, 844.

[3] *W. H. F. Sasse*, *T. Teitei*, and *D. Wells* in Book of Contributed Papers, Euchem Research Conference on Useful Preparative Aspects of Photochemistry, Ghent (Belgium) 1975.

[4] *G. Kaupp*, lecture at Chemiedozententagung at Regensburg, April 2, 1976. The Woodward-Hoffmann Rules and Thereafter. Universität Freiburg (Germany), 1974/75.

[5] All the corrected excitation spectra are superposable on the UV spectra above 270 nm (UV in ether/ethanol = 1:2 at −190°C: λ_{max} = 236, 248, 273, 282 sh, 304 sh, 314, 320 sh, 328, 333 sh).

[6] *R. Criegee*, Angew. Chem. *87*, 765 (1975); Angew. Chem. Int. Ed. Engl. *14*, 745 (1975); the structure of *(6)* follows from the analytical and spectroscopic data of the ester obtained with diazomethane.

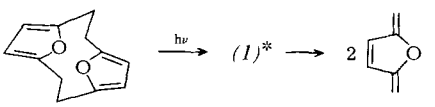
[7] *G. Kaupp*, Angew. Chem. *88*, 482 (1976); Angew. Chem. Int. Ed. Engl. *15*, 442 (1976).

[6+6] Photocleavage of [2.2]Cyclophanes[**]

By *Gerd Kaupp*[*]

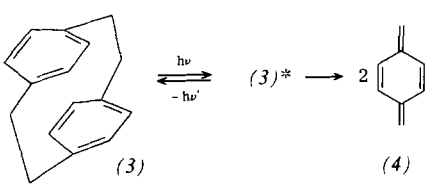
Photochemical [6+6] reactions are of significance as higher members of the cyclovinylogous series of two-step multicenter reactions[1a]. Their success is tied to important conformational conditions. Thus both unproductive radiationless deactivation by conformational changes (such as internal rotation or inversion) and excessive competition from simpler reaction types in smaller sections of the 12-electron system must be avoided. With suitable [2.2]cyclophanes these conditions can be satisfied by restriction of the conformational flexibility and incorporation of the conjugated double bonds in largely planar rings[1b]. We now report new photocleavages of the phanes *(1)*, *(3)*, and *(6)* which confirm these arguments.

[2.2](2,5)Furanophane *(1)*[2] exists in the relatively rigid step-type conformation, as shown by molecular models. Its UV spectrum [cyclohexane: $\lambda_{max}(\varepsilon)$ = 223 (15000), 231 (sh, 10200), 238 (sh, 2740), 246 nm (sh, 1220)] permits excitation with a low pressure mercury lamp. Irradiation (20 or −190°C) is seen to lead to a very rapid build-up of UV spectra corresponding to those of 2,5-dimethylene-2,5-dihydrofuran *(2)*[2a] which can be isolated at −78°C [ether/ethanol = 1:2; 25°C, λ_{max} = 231 sh, 288 sh, 296, 305 sh; −190°C: λ_{max} (E_{rel}) = 232 (0.68), 278 (sh, 0.51), 290 (sh, 0.79), 299.5 (1.00), 312 nm (0.77)]. These spectra are stable for several hours at 25°C and also survive brief irradiation with 313 nm light. No processes competing with [6+6] photocycloreversion of *(1)*, such as fluorescence, can be observed ($\Phi_{Fl} < 10^{-5}$); an isosbestic point is registered at 229 nm.

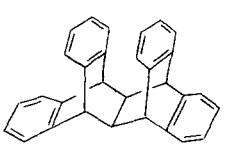


(1) *(2)*

Also in the case of [2.2]paracyclophane *(3)* conformational conditions appear favorable for [6+6] photocleavage to give *p*-quinodimethane *(4)*. On the other hand, transannular interactions are apparent from the UV spectrum[3]. The excimer character of long-wave excited *(3)* is revealed also by an unstructured fluorescence (cyclohexane: $\lambda_{max}^{corr.}$ = 355 nm, Φ_{Fl} = 0.0081)[4]. Substantiation of these concepts comes from the fluorescence of sterically fixed janusene *(5)*[5] having two parallel benzene rings separated by 2.5 Å. As for *(3)* it is unstructured (cyclohexane: $\lambda_{max}^{corr.}$ = 343 nm, Φ_{Fl} = 0.0025; ether/ethanol, −196°C: 340 nm) and thus supplements observations made for *(6)*[6].



(3) *(4)*



(5)

On long-wave excitation of *(3)* (300, 313 nm) no [6+6]cleavage to give *(4)* is observed. Only short-wave excitation leads to [6+6] cycloreversion, albeit significantly more slowly than in the case of *(1)*. At −190°C in ether/ethanol = 1:2 this reaction is manifested directly by the appearance of reproducible UV spectra of *(4)*. The suspected two-step nature of the reaction is confirmed above all by the structure of open-chain alcohol adducts obtained from *(3)* at room temperature[7].

The UV spectra of *(4)* which can now be conveniently recorded lie at much longer wavelengths than those recorded in the gas phase[8a]. Nor do they possess the unstructured bell shape, which has meanwhile been theoretically interpreted, found from film spectra recorded after vacuum pyrolysis of

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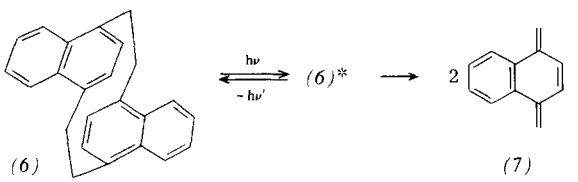
(3)[8b]. It is especially fortunate that ether/ethanol solutions of *(4)* are sufficiently stable after thawing to *ca.* 20°C to permit recording of several UV spectra. Within about 3 h the concentration of *(4)* falls by one half; after 20 h regeneration of *(3)* is complete [20°C; spectral resolution 0.5 nm: λ_{max} (E_{rel}) = 269 (sh, 0.48), 282 (0.78), 292 nm (1.00); −190°C: λ_{max} = 243 sh, 268 sh, 274 sh, 277 sh, 281 sh, 285.5, 289 sh, 293 sh, 298.5 nm]. The assignment of these spectra with the most intense first partial vibrational band to *(4)* is supported by the UV spectrum of 3,6-dimethylene-1-cyclohexene [cyclohexane: 256 (sh, 25200), 264 (30000), 274.5 nm (21200)[9]] and corresponding differences in several linear and branched conjugated azapolyenes, merocyanines, and diketones of the same type[10].

In the same way as *(4)*, compound *(7)* can be prepared by short-wave irradiation (253.7 nm) of *(6)* at −190°C in ether/ethanol = 1:2 (isosbestic points at 256.5 and 313 nm; concerning long-wave irradiation, see ref. [6]). Compound *(7)* is more stable than *(4)* (*ca.* 30% disappearance in 20 h at



(6) *(7)*

25°C). Again it does not display a bell-shaped absorption spectrum[8b, 11] but a clearly structured one with a most intense first partial vibrational band (−190°C: λ_{max} = 258 sh, 269.5, 278 sh, 282, 293.5, 304 sh, 307; 20°C: 267, 280 sh, 291, 303 nm), and is photolabile like *(4)* at elevated temperatures.

In order to prepare *(4)* and *(7)* the reaction medium must still be "fluid". Thus the [6+6] cleavage cannot be performed in EPA at −196°C apparently because the cleavage products cannot diffuse apart in the hard glass. The convenient mode of preparation and the unexpectedly high thermal stability of *(2)*, *(4)*, and *(7)* suggest use of these compounds for cycloadditions.

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(1), 5088-46-0; *(2)*, 13314-90-4; *(3)*, 1633-22-3; *(4)*, 502-86-3; *(6)*, 17341-02-3; *(7)*, 7545-39-3

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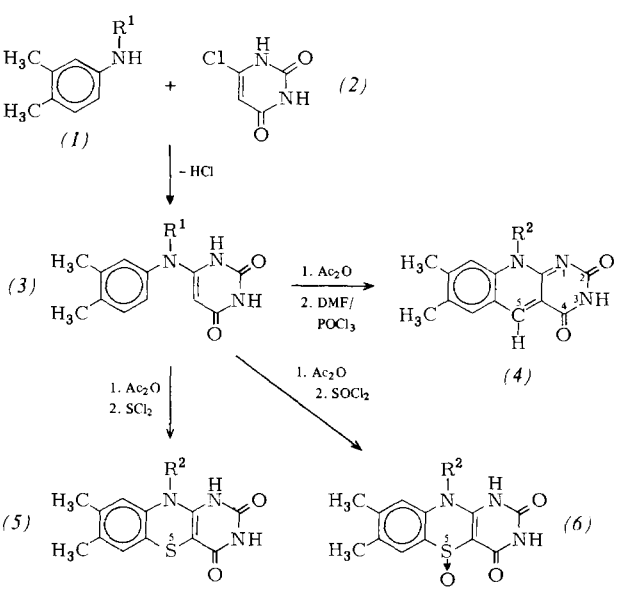
[11] Cf. also the spectra of dibenzo-*p*-quinodimethane [ether/ethanol, −190°C: λ_{max} (E_{rel}) = 238, 241 sh, 245 sh, 248 sh, 253 sh, 256 sh, 263, 277 (sh, 0.69), 287 (0.97), 299 (1.00); fluorescence: $\lambda_{max}^{corr.}$ (Q_{rel}) = 338 (sh, 0.59), 403 (1.00), 423 (0.83), 450 (sh, 0.44)] [10].

5-Deaza- and 5-Thiariboflavins: A Simple Pathway to Antimetabolites of Vitamin B_2

By *Michael Janda* and *Peter Hemmerich*[*]

The flavocoenzymes derived from vitamin B_2 are vital components of all biological redox chains, animal respiration, plant photosynthesis, and microbial oxygenation (detoxification)[1]. Flavoproteins are unique as switch-over units between hydride and electron transfer; moreover, they compete with hemoproteins in oxygen activation. A relationship between these seemingly unrelated types of activity is revealed by the fact that the $2e^{\ominus}/H^{\ominus}$-conversion, like the reduction of the triplet $^3O_2$, involves spin coupling and decoupling, *i.e.* a forbidden non-conservation of multiplicity. That the chemistry of the flavin-dependent biological oxidoreduction has only recently become fully understood probably lies in the fact that *in vivo* and/or *in vitro* active vitamin B_2 antimetabolites were hardly known.

5-Deazaflavocoenzymes *(4)*, R^2 = ribityl phosphate, have recently been employed for the modification of flavoproteins[2]. 5-Deazaflavoproteins retain the ability to transfer $H^{\ominus}$, *i.e.* the (de)hydrogenation activity, even if to a small extent, but $e^{\ominus}$-transfer and O_2-reduction are completely blocked[3]. It is obvious that the essential biocatalytical difference between the natural flavocoenzyme and its 5-deaza modifications is not to be found in the oxidized state but in the half- and fully-reduced states[4]. To facilitate access to 5-deazariboflavins, we have sought a simple direct synthesis which at the same time can be used for introduction of sulfur in position 5 of the flavin. The 5-thiaflavins *(5)* and *(6)* thus formed act equally strongly on *Phycomyces*[5] as the deaza compounds. We presume—conversely to the situation in 5-deazaflavins—that the $e^{\ominus}$ transferability remains, while $H^{\ominus}$-transfer and O_2-reduction are blocked.



R^1 = Ribityl; R^2 = Tetraacetylribityl

Since the well known synthesis of deazaflavin[6] is tedious and, for ribityl derivatives, very unproductive, we resorted to a new method of flavin synthesis first reported by *Yoneda et al.*[7]. Ribitylxylidine *(1)* (Hoffmann-La Roche, Basel) was condensed with 6-chlorouracil *(2)* and the resulting product *(3)* reacted with DMF/$POCl_3$, SCl_2, or $SOCl_2$ directly after

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acetylation to yield the flavin analogs *(4)*, *(5)*, or *(6)*, respectively, in good yields; they can be converted into the ribityl derivatives by deacetylation.

5-Deazariboflavin (4), $R^2=R^1$

A solution of 6-[*N*-(tetraacetyl-D-ribityl)-3,4-xylidino]uracil *(3)*, $R^1=R^2$, (2.50 g, 4.7 mmol) in DMF (8 ml) is treated with $POCl_3$ (0.80 ml, 8.7 mmol). The mixture is allowed to stand for 30 min at room temperature and for 15 min at 100 °C. It is then poured onto ice, adjusted to pH = 6 with ammonia at 0 °C, and stirred for 30 min. The product is filtered off, and washed with a large volume of water. After drying over P_2O_5, 2.30 g (91 %) of *(4)* is obtained. Deacetylation in 50 % saturated methanolic ammonia solution yields 1.10 g (62 %) *(4)*, $R^2=R^1$, which is thin-layer chromatographically and spectrally identical with authentic material[6].

5-Deaza-5-thia-1H-riboflavin (5), $R^2=R^1$

A solution of *(3)*, $R^1=R^2$, (3.7 mmol) in $CHCl_3$ (5 ml) is treated with SCl_2 (0.50 ml, 7.8 mmol) and stirred for 12 h at room temperature. The solvent is then removed *in vacuo* and the residue taken up in 10 ml DMF. This solution is added dropwise and slowly to 100 ml of a 0.1 M solution of $Na_2S_2O_4$ in 0.1 M phosphate buffer (pH = 7). After complete decoloration the solution is extracted three times with 100 ml $CHCl_3$ and the $CHCl_3$ removed *in vacuo*. The residual oil crystallizes upon addition of diethyl ether; yield 1.30 g (62 %) *(5)*. Deacetylation in 20 ml saturated methanolic ammonia solution affords 0.64 g (44 %) *(5)*, $R^2=R^1$. ^{1}H-NMR (1 N K_2CO_3 in D_2O): $\delta=2.05$ (s, 7,8-CH_3, 6H), 3.52—4.28 (m, 10-ribityl, 7H) and 6.50–6.75 ppm (6,9-CH, 2H); UV: pH = 13, anion, λ_{max} (ε) = 262 (27720), 298 sh (8320), 316 nm sh (3170); pH = 2, neutral entity, λ_{max} (ε) = 252 (18610), 280 sh (9590), and 345 nm sh (1980); $pK = 5.3 \pm 0.1$.

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(1), 3051-94-3; *(2)*, 4270-27-3; *(3)*, 36995-92-3; *(3)* ($R^1=R^2$), 59389-71-8; *(4)*, 59389-72-9; *(4)* ($R^2=R^1$), 19342-73-5; *(5)*, 59389-73-0; *(5)* ($R^2=R^1$), 59389-74-1; *(6)*, 59389-75-2

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4,6-Diphenylthieno[3,4-*d*][1,3]dioxol-2-one 5,5-Dioxide, A Novel Activating Agent for Peptide Syntheses[**]

By *Oswald Hollitzer, Alfred Seewald*, and *Wolfgang Steglich*[*]

4,6-Diphenylthieno[3,4-*d*][1,3]dioxol-2-one 5,5-dioxide *(2)*, which is readily accessible by reaction of the sulfone *(1)*[1] with phosgene/pyridine, is of preparative interest as a doubly activated cyclic carbonic ester [IR(KBr): $\nu_{CO} = 1895\ cm^{-1}$].

We have found that *(2)* reacts smoothly with carboxylic acids and pyridine in anhydrous aprotic solvents to give the esters *(3)* (Table 1), which as mixed anhydrides of a vinylogous sulfonic acid [IR (KBr): $\nu_{CO} = 1780$—1775 and $1720\ cm^{-1}$] are excellent acyl transferring agents. Simple esters *(3)* can also be prepared directly from *(1)* by the usual acylation methods, but *(2)* is to be preferred in the case of *N*-acylamino acids because of the higher yields and mild reaction conditions.

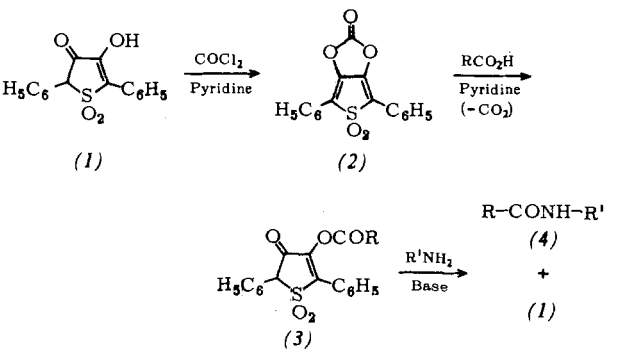
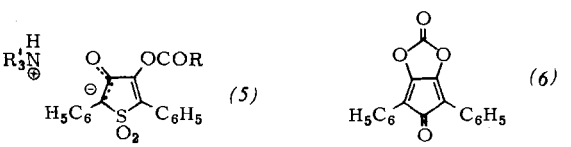


Table 1. 4-Acyloxy-3-oxo-2,5-diphenyl-2,3-dihydrothiophene 1,1-dioxide *(3)* [a].

Cpd.	RCO	Yield [%] [b]	Method [c]	M.p. [°C] [d]	$[\alpha]_{546}^{25}$ [°] [d]
(3a)	H_5C_2CO	70	C	101—102	—
(3b)	$(CH_3)_3CCO$	91	C	177—178	—
(3c)	Z-Val	95	A	161—163	43.5
		82	B		
(3d)	Z-Pro	99	A	104—106	54.3
(3e)	Boc-Pro	98	A	158—159	55.7
(3f)	Boc-Phe	96	A	170	39.0
(3g)	Boc-Met	91	A	193—194	37.4

[a] All compounds gave correct elemental analysis.
[b] Crude yields of spectroscopically pure compounds.
[c] A: from carboxylic acid, pyridine and *(2)*; B: from carboxylic acid, *(1)* and dicyclohexylcarbodiimide; C: from carboxylic acid chloride, *(1)* and pyridine.
[d] Values for recrystallized analytically pure compounds. *(3c)*—*(3g)* are present as diastereoisomeric mixtures. [α]: $c = 1$ in dichloromethane.

The activated esters *(3)* are easily crystallizable, stable compounds which on reaction with amines in the presence of 1 mol pyridine or triethylamine readily afford the amides *(4)*. Addition of base prevents retardation of the reaction by the liberated acidic sulfone *(1)*[2]. Particularly advantageous is that on addition of the amine components, the esters *(3)* form orange-red anions *(5)*[3] whose disappearance, accompanied by a color change to pale yellow, indicates completion of reaction. The sulfone *(1)* formed along with the amide *(4)* is easily removed by extraction with aqueous hydrogen carbonate[4]. The activation with *(2)* and the amide coupling to *(4)* can also be carried out as a single vessel reaction without isolation of the activated ester *(3)*.



As shown in Table 2, sterically demanding dipeptide derivatives *(4)* are also formed in almost quantitative yields within

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[**] This work was supported by the ERP Sondervermogen.

a few minutes. The products were characterized without resort to recrystallization and in most cases were analytically pure. A gas-chromatographic investigation of the *N*-trifluoroacetyl-Pro-Val methyl ester[5] revealed that activation and peptide coupling proceeds without racemization in the case of Z-Pro-Val-OMe[6].

Table 2. *N*-Acyldipeptide esters *(4)* [a].

(4)	Reaction time [min] Base employed	Yield [%]	M.p. [°C] [Lit.-m.p.]	Ref.
Z-Val-Val-OMe	120, triethylamine	97	104 [107—109]	[7]
Z-Pro-Val-OtBu	10, pyridine	94	111—112 [114—115]	[8]
	120, triethylamine	97	112—114 [c]	
	60, pyridine	94	107—111	
Boc-Phe-Val-OMe	15, triethylamine	93	110—112 [120—122] [d]	[9]
Boc-Met-Ala-OMe	120, triethylamine	99	72 [87—88]	[10]

[a] Yield and m.p. of crude products after drying in an oil-pump vacuum.
[b] Without isolation of *(3d)* after 60 min preactivation of benzyloxycarbonylproline (Z-Pro) with *(2)* and pyridine.
[c] $[\alpha]_D^{20} = -34.0°$ (Ref. [8]: $-34.3°$); $c = 1$ in DMF.
[d] $[\alpha]_D^{25} = -11.1°$ (Ref. [9]: $-11°$); $c = 0.5$ in DMF.

Competing experiments demonstrate that the esters *(3)* are more effective acyl transferring agents than the *p*- and *o*-nitrophenyl esters commonly employed in peptide syntheses[11]. Thus, after 2 h at room temperature an equimolar mixture of *(3b)*, *p*-nitrophenyl acetate, and benzylamine in THF yields 97% *N*-benzylpivalamide and 3% *N*-benzylacetamide (NMR and GC analysis) even though *(3b)* is sterically grossly disfavored. On reaction of *(3a)* and *o*-nitrophenyl acetate with valine methyl ester in THF a mixture of 99% *N*-propionyl derivative and only 1% *N*-acetyl derivative is formed. We attribute the high activity of the ester *(3)* towards amines to the fact that the enolate group in the anion accelerates the aminolysis by intramolecular base catalysis[12].

In principle the peptide synthesis can also be carried out with 4,6-diphenylcyclopenta[*d*][1,3]dioxol-2,6-dione, which can be prepared analogously to *(2)* from 4-hydroxy-2,5-diphenyl-4-cyclopenten-1,3-dione[13], phosgene, and pyridine [*(6)*: black-violet crystals which decompose above 100°C without any definite melting point; IR (KBr): $\nu_{CO} = 1890$ cm^{-1}].

4,6-Diphenylthieno[3,4-d][1,3]dioxol-2-one 5,5-dioxide (2)

A 20% solution of phosgene in toluene (≈ 0.2 mol) is added dropwise at 20°C to a vigorously stirred solution of 4-hydroxy-3-oxo-2,5-diphenyl-2,3-dihydrothiophene 1,1-dioxide *(1)*[1] (30 g, 0.10 mol) and pyridine (17 ml, 0.21 mol) in dry tetrahydrofuran (600 ml). After 1 h the precipitated pyridinium chloride is filtered off and the filtrate freed of excess phosgene by passage of a stream of dry nitrogen. The filtrate is then concentrated to 2/3 of its original volume, refiltered, and finally concentrated further until crystallization of *(2)* takes place. After allowing to stand for several hours at 0°C, 24 g (73%) of yellow-green fluorescing needles crystallize out which decompose at >250°C. *(1)* can be recovered from the concentrated mother liquor by addition of sodium hydroxide, filtration, and subsequent acidification.

Activated ester (3f) of N-tert-butoxycarbonyl-L-phenylalanine

A mixture of *(2)* (1.96 g, 6.0 mmol), Boc-Phe-OH (1.33 g, 5 mmol), and pyridine (0.49 ml, 6.0 mmol) in anhydrous dichloromethane (50 ml) is stirred for 2 h (evolution of CO_2!). The mixture is washed three times each with 20% citric acid solution and saturated $NaHCO_3$ solution, then once more with citric acid and water. After drying over $MgSO_4$ and evaporation in a vacuum 2.63 g (96%) of the desired compound is obtained (m.p. 169°C; after recrystallization from ethyl acetate/petroleum ether, m.p. 170°C).

N-tert-Butoxycarbonyl-L-phenylalanyl-L-valine methyl ester of type (4)

To the red-orange solution of *(3f)* (1.10 g, 2.0 mmol) and triethylamine (0.61 g, 4.4 mmol) in anhydrous dichloromethane (50 ml) is added valine methyl ester hydrochloride (0.40 g, 2.4 mmol), whereupon the color changes immediately to pale yellow. The mixture is stirred for 15 min at 20°C and worked-up as in the case of *(3f)*. Yield 0.70 g (93%).

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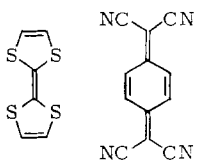
(1), 54714-10-2; *(2)*, 54714-11-3; *(3a)*, 54714-12-4; *(3b)*, 54714-13-5; *(3c)*, isomer a, 54750-86-6; *(3c)*, isomer b, 54750-87-7; *(3d)*, isomer a, 54714-14-6; *(3d)*, isomer b, 54714-15-7; *(3e)*, isomer a, 54714-16-8; *(3e)*, isomer b, 54714-17-9; *(3f)*, isomer a, 54714-18-0; *(3f)*, isomer b, 54714-19-1; *(3g)*, isomer a, 54714-20-4; *(3g)*, isomer b, 54714-21-5; *(6)*, 54714-22-6; H_5C_2COCl, 79-03-8; $(CH_3)_3CCOCl$, 3282-30-2; Z-Val-Val-OMe, 1999-88-8; Z-Pro-Val-O-*t*-Bu, 26061-29-0; Boc-Phe-Val-OMe, 2754-02-1; Boc-Met-Ala-OMe, 18670-99-0; Z-Val-OH, 1149-26-4; Z-Pro-OH, 1148-11-4; Boc-Pro-OH, 15761-39-4; Boc-Phe-OH, 13734-34-4; Boc-Met-OH, 2488-15-5

[1] *C. G. Overberger, S. P. Ligthelm,* and *E. A. Swire,* J. Amer. Chem. Soc. *72*, 2856 (1950); *M. Chaykovsky, M. H. Lin,* and *A. Rosowsky,* J. Org. Chem. *37*, 2018 (1972).
[2] $pK_a \approx 4.3$; cf. *R. H. Eastman* and *R. M. Wagner,* J. Amer. Chem. Soc. *71*, 4089 (1949).
[3] The color intensity corresponds to the basicity of the amine: alkylamines > amino acid ester ≫ pyridine. On combined addition of *(3b)* with dicyclohexylamine in tetrahydrofuran an orange salt of type *(5)* precipitates out [m.p. 205—207°C, IR (KBr) $\nu_{CO} = 1756$ cm^{-1}]. In $CHCl_3$ two carbonyl bands appear at 1760 and 1718 cm^{-1}; hence at least some free *(3b)* must be present.
[4] *(1)* can be recovered by acidification of the aqueous phase and used for further preparation of *(2)*.
[5] *F. Weygand, A. Prox, L. Schmidhammer,* and *W. König,* Angew. Chem. *75*, 282 (1963); Angew. Chem. internat. Edit. *2*, 183 (1963).
[6] In the synthesis of Boc-Leu-Phe-Val-OtBu from Boc-Leu-Phe-OH, *(2)* and H-Val-OtBu, considerable racemization takes place. *W. König,* Hoechst AG, private communication.
[7] *W. König* and *R. Geiger,* Chem. Ber. *103*, 2034 (1970).
[8] *W. König* and *R. Geiger,* Chem. Ber. *103*, 788 (1970).
[9] *O. Goffredo, L. Bernardi, G. Bosisio,* and *F. Chillemi,* Gazz. Chim. Ital. *95*, 172 (1965).
[10] *C. Schattenkerk, I. Voskuyl-Holtkamp,* and *R. Bokhorst,* Rec. Trav. Chim. Pays-Bas *92*, 92 (1973).
[11] *M. Bodanszky, K. W. Funk,* and *M. L. Fink,* J. Org. Chem. *38*, 3565 (1973) and previous work.
[12] Cf. summary by *J. H. Jones,* Chem. Ind. (London) *1974*, 723.
[13] *L. Claisen* and *Th. Ewan,* Liebigs Ann. Chem. *284*, 245 (1895).

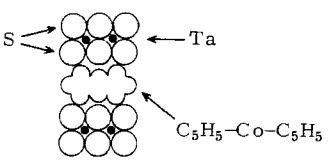
Reviews

Abstracts of selected progress reports and review articles

The electronic properties of some chain and layer compounds are reviewed by *A. D. Yoffe*. Solids having a chain or layer structure can be regarded as "one"- or "two-dimensional" solids if the distance between the molecular units lies in the order of magnitude of van der Waals radii. This leads to very strong anisotropy in electronic and mechanical behavior as well as in vibrational properties. Examples of conductive solids having metal-like chains are the charge transfer complex *(1)*, the polymer $(SN)_x$ and the complex



(1)



(2)

$K_2Pt(CN)_4Br_{0.3}\cdot 3H_2O$, which contains linear chains of platinum atoms. In the case of layer compounds the transition metal dichalcogenides MX_2 with molecules or atoms incorporated in them are of special interest. Metallocenes behave as pseudoalkali metals, *e.g.* in *(2)*. [Electronic Properties of Some Chain and Layer Compounds. Chem. Soc. Rev. *5*, 51—78 (1976); 52 references]

[Rd 856 IE—F]

The oxidation of organic compounds with active MnO_2 is the subject of a two-part review by *A. J. Fatiadi*. MnO_2 is a mild reagent for the heterogeneous oxidation of alcohols and hydroxy compounds (unsaturated and saturated aliphatic alcohols, benzyl alcohols, heterocyclic alcohols, polyhydroxy compounds, carbohydrates, phenols), terpenes, steroids and alkaloids. The reaction conditions for the synthetic use of active MnO_2, the selectivity and specifity of MnO_2 as oxidizing agent, and the mechanisms of oxidation (free radical and ionic) are discussed. In the second part the author deals with the use of MnO_2 in benzilic acid type rearrangements, selective dehydrogenation reactions (*e.g.* in steroids and N-heterocycles), and the aromatization of carbocyclic and heterocyclic compounds. MnO_2 is an interesting reagent for the oxidation of primary, secondary, and tertiary amines and amine derivatives (hydroxylamine, oximes, hydrazine, hydrazides, azines, and hydrazones). Also dealt with are, *inter alia* the oxidation of nitriles, indoles, carbazoles, as well as the oxidative dimerization of heterocyclic compounds. [Active Manganese Dioxide Oxidation in Organic Chemistry. Synthesis *1976*, 65—104, 133—167; 697 references]

[Rd 858 IE—M]

The role of membrane proteins in anion transport in erythrocytes is dealt with in an article by *A. Rothstein, Z. I. Cabantchik*, and *P. Knauf*. As is known from affinity labelling experiments, anionic inhibitors of anion transport bind themselves to a membrane protein of molecular weight 100000, which is known as band 3. In part, this protein is exposed on the membrane, and with the aid of hydrophobic amino acid side chains partly interacts with membrane lipids. A model is proposed in which this protein serves as a channel for migration of the anions through the lipid double layer. A binding site for anions at the external exit of this channel is thought to make an anion exchange through a diffusion barrier possible by a local conformational transformation. [Mechanism of Anion Transport in Red Blood Cells: Role of Membrane Proteins. Fed. Proc. *35*, 3—10 (1976); 61 references]

[Rd 859 IE—R]

Biochemical aspects of the toxicology of cadmium are reviewed in an article by *R. L. Singhal, Z. Merali*, and *P. D. Hrdina*. It is known that cadmium accumulates in certain target organs *e.g.* liver and kidney, in which histological alterations are also detectable. In particular the influence of cadmium on the carbohydrate metabolism of the liver, as well as on the adrenal cortex, prostate, testes, pancreas and brain of the rat has been investigated. In most cases the alteration of metabolism lasts up to 28 days after termination of cadmium treatment. [Aspects of the Biochemical Toxicology of Cadmium Fed. Proc. *35*, 75—80 (1976); 51 references]

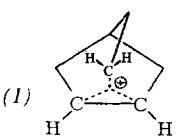
[Rd 860 IE—R]

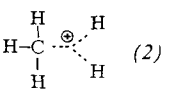
The metabolism of xenobiotica in the lung is the subject of an article by *E. Bingham, R. Niemeier*, and *W. Dalbey*. In this system—isolated lung perfused with autologous blood—benzo[a]pyrene affords the corresponding 3-hydroxy compound, three dihydrodiols and, in a yield amounting to 50% of all metabolites formed, an unidentified polar compound. Pretreatment with 3-methylcholanthrene accelerates the metabolization and slightly alters the product pattern. [Metabolism of Environmental Pollutants by the Isolated Perfused Lung. Fed. Proc. *31*, 81—84 (1976); 19 references]

[Rd 861 IE—R]

The σ-bridged 2-norbornyl cation *(1)* and its significance to chemistry is the title of a survey by *G. A. Olah*. The carbocation *(1)* is an example of carbon compounds having two-electron three-center bonds; in order to distinguish it from the "classical" carbenium ions of type CR_3^+ having normal two-electron two-center bonds it is called a "nonclassical" ion. The parent compound is the methonium ion *(2)*, a pentacoor-

(1)





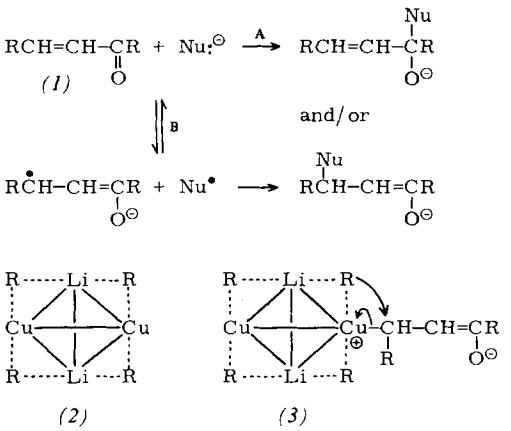
(2)

dinated carbonium ion. After an introduction to the norbornyl problem and a survey of the state of solvolytic investigations, as well as a discussion of NMR, Raman, ESCA, and equilibrium studies, the author states that there is no such thing as a perfectly "classical" carbocation; there is always some degree of delocalization. [The σ-Bridged 2-Norbornyl Cation and Its Significance to Chemistry. Acc. Chem. Res. *9*, 41—52 (1976); 49 references]

[Rd 862 IE—L]

Additions of lithium organocuprates as models for electron-transfer processes are the topic of a review by *H. O. House*. The addition of nucleophiles $Nu:^-$ to unsaturated carbonyl compounds *(1)* (or other electrophiles) can proceed *via* path

A (one step) or path B; in path B only one electron is transferred in the first step. The lithium organocuprates $R_4Cu_2Li_2$ (R = *e.g.* CH_3) *(2)*, which are probably dimeric, apparently react with unsaturated carbonyl compounds *(1)* exclusively *via* path



B. *(3)* might be formed as intermediate. [Use of Lithium Organocuprate Additions as Models for an Electron-Transfer Process. Acc. Chem. Res. 9, 59—67 (1976); 34 references]

[Rd 864 IE—L]

Crystals and long-chain molecules are considered by *L. Mandelkern*. Long-chain molecules having sufficiently regular structure, *e.g.* polyethylene, can form three-dimensional arrangements worthy of the name crystals. Crystallization from diluted solution leads to lamellae 100—200 Å thick and several µm long and wide. Their interfaces are amorphous. Crystallized melts are also made up of lamellae whose thickness can vary between several hundred and several thousand Å. A model of a crystallite is proposed in which a lamellar-type ordered structure is covered by an intermediate layer of moderate order followed by an amorphous layer. [Crystals and Long-Chain Molecules. Acc. Chem. Res. 9, 81—86 (1976); 36 references]

[Rd 865 IE—L]

BOOK REVIEWS

Atom-Absorption-Spektroskopie (Atomic Absorption Spectroscopy). By *B. Welz*. Verlag Chemie, GmbH, Weinheim 1975, 2nd completely revised edit., xii, 296 pp., 73 figs., 46 tables, bound, DM 68.—.

After a brief introduction to the physical basis of atomic absorption spectroscopy (AAS) the first part of this book consists of an extensive description of experimental methods and instrumentation; the construction of atomic absorption spectrometers, the use of various primary light sources, possible methods of atomization, as well as the optics and signal registration of the apparatus are described. The second part, which deals with the analytical applications, contains at first general instructions concerning operating techniques and possible sources of interference, and then, separately for each element, special indications for favorable working conditions, these being in some cases supplemented by information about interference and preparation of the samples. Indirect methods for the determination of some compounds and nonmetals are included. A relatively large space is devoted to methods of investigation for specialized areas of application, *e.g.* medicine, geochemistry, metallurgy, petrochemistry, and food and water analysis; in these cases detailed experimental instructions are largely omitted, the reader being referred to the very rich original literature (in all, 1388 references are cited). Finally, in an Appendix, there is a brief comparison of the design of most commercial atomic absorption spectrometers.

The book considers the state of knowledge about AAS up to about the end of 1974. In comparison with the first edition, the work has been extended mainly in the field of flameless procedures, which have gained greatly in importance in recent years. It is particularly welcome that the author describes not only the determination of individual elements on this instrument but also the preparation of the samples, for this is often the major part of the analytical problem. Summarizing, the book can be recommended to all concerned with AAS as a method of analysis. Indeed, it is the only book so far on this subject that has appeared in German.

Reinhard Höhn [NB 318 IE]

Elektrochemie I (Electrochemistry I) (taschentext 41). By *C. H. Hamann* and *W. Vielstich*. Verlag Chemie, GmbH, Weinheim 1975. 1st edit., x, 192 pp., 58 figs., 18 tables, paperback, DM 26.80.

This book from the "taschentext" series deals with the classical fields of electrochemistry, namely electrolytic conduction, electrode potentials from a thermodynamic point of view, and the properties of the electrode/electrolyte phase boundary (models of the electrochemical double layer). It is intended primarily for students who will value the terse way in which the subject is treated.

It is very useful to have an indication of numerical orders of magnitude, *e.g.* in the conductivity table on p. 25.

The relatively detailed discussion of liquid potentials, to which a separate chapter is devoted, is highly welcome, being justified by the importance of these quantities for exact potential measurements. Simple applications of conductivity and potential measurements are treated separately. Electrochemistry in nonaqueous solvents is also considered.

The authors place emphasis on a clear statement of concepts, and in this they have been very successful. In this connection, however, the definition of an ionic conductor on p. 6, which corresponds rather to the exceptional case, should be reconsidered. The simple relationship $\lambda = F \cdot b$ between the ionic equivalent conductivity λ and the mobility b should if possible be placed at the beginning of Chapter 2. The quality and production of the book are such that one awaits with impatience the second volume, in which modern areas such as electrode kinetics, batteries, and organic electrosyntheses will be treated.

Fritz Beck [NB 319 IE]

Dynamic Nuclear Magnetic Resonance Spectroscopy. Edited by *L. M. Jackman* and *F. A. Cotton*. Academic Press, Inc., New York 1975. 1st edit., xiv, 660 pp., numerous figs., and tables, bound, $ 48.00.

The importance of NMR spectroscopy as a method of studying chemical kinetics has long justified a special mono-

graph reviewing the achievements. As editors, *L. M. Jackman* and *F. A. Cotton* have made such an attempt, in which contributions on the technique and application of NMR spectroscopy to time-dependent phenomena are collected under the concept of "dynamic NMR spectroscopy". After an introduction by *H. S. Gutowsky* (22 pp.), *W. G. Klemperer* treats the relationships between reaction mechanisms and NMR exchange processes (22 pp.), and *G. Binsch* describes line shape analysis (38 pp.). There follow two chapters on pulse spectroscopy with applications to exchange processes by *L. W. Reeves* (48 pp.) and measurement of relaxation times by *R. Freeman* and *H. D. W. Hill* (32 pp.). The remainder of the volume is devoted to phenomena that have been brought to light by means of dynamic NMR spectroscopy; rotations around single bonds (*S. Sternhell*, 40 pp.), rotation around partial double bonds (*L. M. Jackman*, 50 pp.), dynamic processes in inorganic and organometallic compounds (*J. P. Jesson* and *E. L. Muetterties*, 64 pp.), in metal chelates (*R. H. Holm*, 60 pp.), in organometallic compounds (*F. A. Cotton*, 64 pp.), in allyl compounds (*K. Vrieze*, 48 pp.), in carbonyl-metal compounds (*R. D. Adams* and *F. A. Cotton*, 34 pp.), in carbenium ions (*A. L. Telkowski* and *M. Saunders*, 20 pp.), in cyclic compounds (*F. A. L. Anet* and *R. Anet*, 78 pp.), and in proton-transfer processes (*E. Grunwald* and *E. K. Ralph*, 28 pp.). This list shows that similar material is not offered in any other place, even if individual subjects have been treated in more detail in specialist monographs. It is only regrettable that there is no chapter on valence tautomerism. It is less painful that there is no contribution on pyramidal inversion, because excellent reviews of this are available. The references are fairly comprehensive up to 1972, and in individual cases also for 1973/74. The experimental results thus remain wholly within the scope of proton-NMR spectroscopy. All in all, this is a book that because of its broad survey of possible applications may interest a wide circle of readers.

Harald Günther [NB 322 IE]

Ullmanns Encyklopädie der technischen Chemie (Ullmann's Encyclopedia of Industrial Chemistry). Edited by *E. Bartholomé, E. Biekert, H. Hellmann, H. Ley* (deceased), and *W. M. Weigert*. Vol. 9: Butadien bis Cytostatica (Butadiene to Cytostatics). Verlag Chemie, GmbH, Weinheim 1975. 4th edit., xvi, 714 pp., 248 figs., 294 tables, subscription price DM 345.—; individual price *ca.* DM 385.—.

This volume of the 4th edition of "Ullmann" is the third in the alphabetical series[*]. Of its 714 pages, 269 are taken up by chlorine and keywords beginning with "Chlor" (chloroacetaldehyde, chloroformic esters, chloramines, chloroacetic acids, chlorohydrocarbons, *etc.*). Other keywords are taken from inorganic chemistry, including the metals cadmium, cesium, calcium, cerium, and chromium with their compounds of industrial interest, also carbides and cyanogen compounds. Mention may also be made of the organic raw materials and chemicals: butene, butadiene, butanols, butyraldehyde, citric acid, caprolactam, aliphatic and aromatic carboxylic acids. When, as in the last-mentioned case, the keyword covers a group of compounds, then the more important representatives of such a group are treated as sub-entries in alphabetic order—for aliphatic carboxylic acids, for example, acetic, formic, and propionic acid are treated in this way. Similarly, pulp and paper are not treated under cellulose (70 pages including the keywords cellulose ethers, esters, and fibers) but are listed individually at other places. Of the pharmaceuticals, chemotherapeutics (43 pages, not including the antibiotics which appeared in vol. 7) and cytostatics (10 pages) can be found. Special keywords include carcinogens (8 pages) and dry cleaning (6 pages).

As in the earlier volumes, subdivision under the individual keywords is effected, whenever possible, in a similar way, which helps the user to find his way in the book. After the introduction the physical and chemical properties are first treated, then production methods and applications. Demands on quality and analysis as well as other practical problems (handling, storage, shipment, environmental questions) are often added. The conclusion is provided by economic aspects and toxicology as well as a list of references.

In the case of keywords that because of their importance are treated in greater detail, *e. g.* chlorine (56 pages), the presentation has the character of a monograph. Thus, among the physical properties of chlorine one finds tables and diagrams, in which (as elsewhere in the new Ullmann) SI units are generally used. For the production of chlorine by electrolysis of sodium chloride—still the most important method—variants of the mercury and the diaphragm process are explained; here the tabular comparisons of the various cell constructions and of the production costs are particularly valuable.

The up-to-date nature of the presentation emerges impressively when in the section on toxicology under the keyword Aliphatic Chlorohydrocarbons one reads what is reported about vinyl chloride; here 10 references are given from 1974 and two from 1975. In this connection it may be noted that for all the keywords the section on toxicology has been provided by *H. Oettel* (Ludwigshafen, Germany).

The new Ullmann no longer needs a special recommendation, and it is to be hoped that the publishers will bring out further volumes in rapid succession.

Ulfert Onken [NB 321 IE]

Das Spiel — Naturgesetze steuern den Zufall (The Game—Natural Laws Govern Chance). By *M. Eigen* and *R. Winkler*. R. Piper & Co. Verlag, Munich—Zurich 1975. 1st edit., 404 pp., 67 colored figs., bound, DM 38.—.

A game book? The game book, namely the book of "Ludus universalis" to "Ludus vitalis" of 1973. What is the nature (physis) of the world? This age-old question, to which the early Greek thinkers of the 6th century B. C. first sought an answer in rational principles (archai), has not lost its topicality during the two and a half millenia that have passed since then. "The Game", within the definition of the Göttingen Nobel prize winner and his associate, gives the (provisionally) final answer: "We see the game as a natural phenomenon that by its dichotomy of chance and necessity lies at the root of all events" (p. 11). "Once begun by elementary particles, atoms and molecules, it is now continued by our brain cells" (p. 18). Thus the "game" principle, with its interrelation between chance and law, is valid equally for nature *and* mind. It is therefore far more than a game of marbles. On the other hand, the expressed emphasis on the complementarity of chance and law in the factual evolutionary game of matter must be firmly borne in mind before accepting one-sided over-evaluation of any individual aspect. Not only waves and corpuscles, natural chance and natural law, and "creation" and "revelation" are complementary, but also the game of nature and the game of the mind, the starting point and the extension. The discussion in this book deals with the validity of the symbolism of the game concept itself and evaluation of its validity beyond the biophysical-chemical framework. All dogmatism is avoided as is all that is blatantly noncommittal: the former is taken care of by the variety of vantage points, the latter by the specific nature of the details. The Eigen-Winkler game principle, even the outline of which can hardly be indicated here, is a fascinating design of ancient

[*] Cf. Angew. Chem. Int. Ed. Engl. *14*, 578 (1975).

simplicity and complex extensibility whose usefulness for universal interpreations has not yet beeneven explored. Let us hope that the spoil-sports do not get busy!

Friedemann Rex [NB 323 IE]

Mathematik für Naturwissenschaftler (Mathematics for Scientists). By *H.-D. Försterling*. Friedrich Vieweg & Sohn, Verlagsgesellschaft, Braunschweig 1975. 1st edit., 289 pp., numerous figs. and tables, paperback, DM 38.—.

While this book is intended for beginner science students, it will also provide anyone who works seriously through it with the theoretical background suited to many scientific problems.

About a third of its length is taken up by problem sets and their solution. The approach to the problems is developed from the text and, whenever possible, supported by graphical presentation. The examples are chosen simply and from all areas of chemistry and physics. Emphasis is always placed on calculation with real quantities *i.e.* with data containing errors or dimensions, which is helpful for the application of the methods explained to practical problems. (However, the way dimensions are applied in the graphical presentations is somewhat unfortunate.) The readily understandable introduction of concepts and definitions is in line with the book's purpose. The author's up-to-date attitude to the aids becoming increasingly available to the scientist is particularly pleasing: computer programs, *xy*-recorder printouts, *etc.* are freely used. The value of analytical solutions of mathematical problems is emphasized, permitting the user to test his ideas rapidly with pocket or desk calculators. Simple numerical methods are also given.

It is difficult to criticize this book which is of a very high standard factually, didactically, and as far as the printing is concerned. Rather, one would like to see an equally intelligible presentation of vector calculus, calculation of errors, and mathematical statistics, since this text is restricted to the properties of functions of one or more variables. It is hoped that wide circulation of this book will not be hindered by its price.

G. Bozler [NB 324 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Reduced Density Matrices in Quantum Chemistry. By *E. R. Davidson*. From the series "Theoretical Chemistry". Edited by *D. P. Craig* and *R. McWeeny*. Academic Press, New York 1976. viii, 135 pp., bound, $ 17.00.

Inorganic Chemistry of the Main-group Elements, Vol. 3. Senior Reporter: *C. C. Addison*. The Chemical Society, London 1976. xi, 536 pp., bound, £ 29.00.—A volume in the series "Specialist Periodical Reports".

Photographic Gelatin II. Published for The Scientific and Technical Group of the Royal Photographic Society. Edited by *R. J. Xox*. Academic Press, New York 1976. xiv, 390 pp., paper, $ 29.75.

Coatings. Recent Developments. By *M. W. Ranney*. Chemical Technology Review No. 64. Noyes Data Corporation, Park Ridge 1976. xii, 313 pp., bound, $ 39.00.

Oxides and Oxide Films, Vol. 4. Edited by *J. W. Diggle* and *A. K. Vijh*. From the series "The Anodic Behavior of Metals and Semiconductors". Marcel Dekker, New York 1976. xiii, 277 pp., bound, SFR. 110.00.

Wissenschaftliche Forschung und elektronische Rechentechnik. By *W. Schulze*. No. 2 of the series "Beiträge zur Forschungstechnologie". Akademie-Verlag, Berlin 1975. xii, 139 pp., paper, *ca.* DM 15.—.

Methods in Carbohydrate Chemistry. Edited by *R. L. Whistler* and *J. N. BeMiller*. Vol. VII: General Methods, Glycosamineglycans, and Glycoproteins. Academic Press, New York 1976. xxi, 293 pp., bound, $ 29.50.

Wörterbuch der Reprographie. Begriffe und Definitionen. Deutsch-Englisch-Französisch/Englisch-Französisch-Deutsch/Französisch-Deutsch-Englisch. Verlag Dokumentation, München 1976. 2nd unrevised reprint of the 3rd completely revised edition. 273 pp., paper, DM 54.—.

Proceedings of the International Conference on Colloid and Surface Science (15 to 20. 9. 1975, Budapest). Vol. 2: Discussions and Free Communications. Edited by *E. Wolfram* and *T. Szekrényesy*. Akadémiai Kiadó, Budapest 1976. vii, 219 pp., bound, DM 26.00.

Arzneiformenlehre. Ein Lehrbuch für Pharmazeuten. By *P. H. List*. Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart 1976. xxvi, 514 pp., bound, DM 62.00.

Biosynthesis, Vol. 4. Senior Reporter: *J. D. Bu'Lock*. The Chemical Society, London 1976. ix, 274 pp., bound, £ 16.00.—A volume in the series "Specialist Periodical Reports".

BAG Farben Lexikon. By *H. Hadert*. BAG Brunner Verlag AG, Zürich/Verlag Chemie, Weinheim 1976. 356 pp., bound, DM 95.00.

Topics in Current Chemistry—Fortschritte der chemischen Forschung. Band 61: Physical and Chemical Applications of Dyestuffs. Springer-Verlag, Berlin 1976. iv, 187 pp., bound, DM 68.00.

Art in Biosynthesis. The Synthetic Chemist's Challenge. Vol. I. By *D. Ranganathan* and *S. Ranganathan*. Academic Press, New York 1976. xi, 249 pp., bound, $ 11.—.

Reviews in Macromolecular Chemistry, Vol. 14A. Edited by *G. B. Butler, K. F. O'Driscoll*, and *M. Shen*. Marcel Dekker, New York 1976. xiii, 344 pp., bound, $ 32.50.

Catalysis Reviews. Science and Engineering, Vol. 12. Edited by *H. Heinemann* and *J. J. Carberry*. Marcel Dekker, New York 1976. xvi, 321 pp., bound, $ 32.50.

Catalysis in Organic Syntheses 1976. Edited by *P. N. Rylander* and *H. Greenfield*. Academic Press, New York 1976. x, 363 pp., bound, $ 16.50.

Inorganic Reaction Mechanisms, Vol. 4. Senior Reporter: *A. McAuley*. The Chemical Society, London 1976. xviii, 398 pp., bound, £ 23.00.—A volume in the series "Specialist Periodical Reports".

Zweisprachiges Wörterbuch für Chemie und Physik mit Anwendungsgebieten. Band 33: Deutsch-Englisch/Englisch-German. Freba-Service, Widnau 1976. 155 pp., paper, DM 24.—.

Vibrational States. By *S. Califano.* John Wiley & Sons, London 1976. xii, 335 pp., bound, £ 16.75.

Experimentelle Einführung in Grundlagen und Methoden der Chemie. By *E. J. Slowinski, W. L. Masterton,* and *W. C. Wolsey.* Gustav Fischer Verlag, Stuttgart 1975. viii, 325 pp., paper, DM 29.80.

The Chemistry of Cyano Complexes of the Transition Metals. By *A. G. Sharpe.* From the series "Organometallic Chemistry". Edited by *P. M. Maitlis, F. G. A. Stone,* and *R. West.* Academic Press, New York 1976. xi, 302 pp., bound, $ 26.25.

Organic Chemistry Series Two. Edited by *D. H. Hey.* Vol. 5: Alicyclic Compounds. Edited by *D. Ginsburg.* From the series "International Review of Science". Butterworths, London 1976. 431 pp., bound, £ 13.45.

Coal Conversion Technology. By *I. Howard-Smith* and *G. J. Werner.* Chemical Technology Review No. 66. Noyes Data Corporation, Park Ridge 1976. xx, 133 pp., bound, $ 24.00.

Structure and Bonding. Edited by *J. D. Dunitz, P. Hemmerich, R. H. Holm, J. A. Ibers, C. K. Jorgensen, J. B. Neilands, D. Reinen,* and *R. J. P. Williams.* Vol. 26: Spectra and Chemical Interactions. Springer-Verlag, Berlin 1976. iv, 144 pp., bound, DM 58.00.

Handbook of Organic Reagents in Inorganic Analysis. By *Z. Holzbecher, L. Diviš, M. Král, L. Šůcha,* and *F. Vláčil.* From the series "Ellis Horwood Series in Analytical Chemistry". Edited by *R. A. Chalmers.* Ellis Horwood, Chichester/John Wiley & Sons, New York 1976. 734 pp., bound, £ 19.00.

Cholinesterases and Cholinergic Receptors. Edited by *E. Reiner.* Proceedings of the International Meeting in Split 1975. Croatica Chemica Acta (Offprint), Zagreb 1975. xii, 344 pp., paper, $ 12.00.

Quantum Chemistry. By *I. N. Levine.* Allyn and Bacon, Boston 1975. 2nd Edit., xii, 506 pp., bound, $ 18.95.

Fine Particles. Aerosol Generation, Measurement, Sampling, and Analysis. Edited by *B. Y. H. Liu.* Academic Press, New York 1976. xiii, 837 pp., bound.

Chemistry and Biochemistry of Plant Pigments. Edited by *T. W. Goodwin.* Academic Press, London 1976. 2nd Edit., Vol. 1: xvi, 870 pp., bound, £ 26.50; Vol. 2: xii, 373 pp., bound, £ 12.00.

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Penetration and Crosslinking of Macromolecules[**]

By Dietrich Braun[*]

One of the topical problems of macromolecular chemistry is the question of the extent to which macromolecules in solution or in the amorphous solid state can engage in mutual interpenetration. The present article is concerned primarily with recent investigations on crosslinking copolymerization and with inter- and intramolecular reactions of polymers as a contribution to the study of molecular shape.

1. Introduction

The question of the shape of macromolecules in highly dilute solution has long been a focal point of physicochemical investigation in the field of polymers[1]. The overall conformation of the molecules can accordingly be described in general in terms of the model of the ideal random coil, provided that interactional forces of constitutional origin between the repeat units do not lead to a higher, *e.g.* helical, order. This special case has been excluded from the following discussion, although it must be pointed out that even completely helical molecules can form random coils at very high degrees of polymerization.

The picture of an ideal random coil with infinitely thin chain has to be modified in practice because real molecules possess a finite thickness and thus occupy a certain volume; this leads to an "excluded volume", which causes some enlargement of the coil relative to the "ideal state", even at infinitely high dilution. Moreover, the location of one molecule is clearly not available to a second one. Therefore the question arises whether a mutual interpenetration of different coils can be achieved in polymer solutions with increasing concentration or whether the individual macromolecules coexist as completely or partially isolated entities (cell model of *Vollmert*[15]; cf. Fig. 1). The related problems are also of importance for the conformation of polymers in the molten and the amorphous solid state; appropriate studies thus possess not only scientific but also considerable practical interest, *e.g.* for film formation from polymer solutions and for the properties of polymeric melts or glasses. Finally, important conclusions about the structure of networks can be drawn from observa-

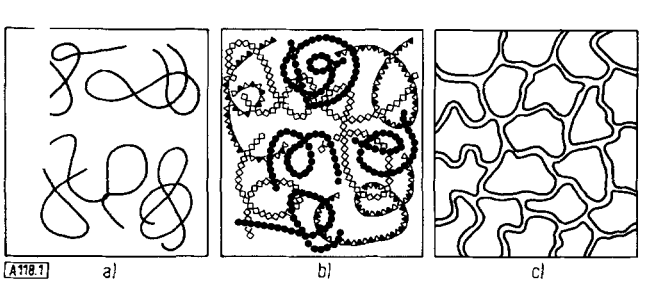

Fig. 1. Schematic representation of the behavior of dissolved macromolecules: a) in highly dilute solutions (particle solution according to *Schurz*[14]); b) on coil interpenetration; c) on hindered interpenetration (cell model of *Vollmert* [15]) or hooking together in the boundary regions of the coils (network solutions according to *Schurz* [14]).

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tions on the curing of duroplastics, *i.e.* crosslinking reactions between linear macromolecules, from their shape in concentrated solutions or melts; a similar situation exists with crosslinking polyreactions. Thus there is also a close relationship between the problem of interpenetration of linear macromolecules and the density of polymeric networks.

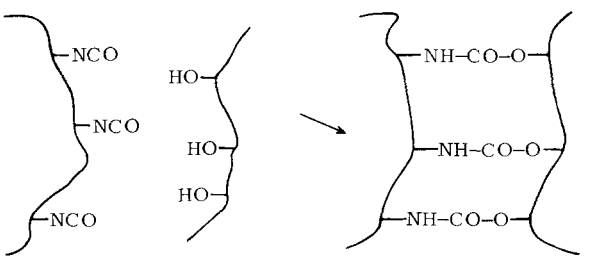
2. Experimental Studies on Coil Interpenetration

While information about the shape and arrangement of chain molecules is available from X-ray studies in the case of partially crystalline solid polymers, this becomes much more difficult for dissolved or amorphous solid polymers. A thermodynamic treatment of polymer solutions according to the Flory-Huggins theory permits deduction of the presence of ideally coiled macromolecules with complete mutual interpenetration[1]. Investigations of aggregation thickness in microheterogeneous block copolymers, light scattering and diffusion of dissolved macromolecules in polymer mixtures, and rheological measurements lead, according to *Hoffmann*[2, 3], to the conclusion that the molecules in amorphous soft polymers and also in normal solution form random, interpenetrating coils. *Pechhold*, on the other hand, has predicted chain molecules to exist as parallel extended bundles of molecules also in the amorphous solid state[4]. In this connection, particular interest attaches to recent work by *Kirste*, who has employed neutron diffraction on mixtures of normal and deuterated amorphous polymers in the solid state and in concentrated solutions to derive information about the size of the coils[5, 6]. Accordingly, the coil dimensions, *e.g.* in solid poly(methyl methacrylate), are practically the same as those measured in low-molecular Θ solvents[*], thus suggesting extensive interpenetration. Other authors[7–9] have also concluded on the basis of various methods of investigation that amorphous polymers form loose, interpenetrating coils.

Opposing evidence comes from some rheological studies[10, 11], whose results can be interpreted by assuming the polymer coils in concentrated solution to preserve the same individuality as in highly dilute systems but with a concentration-dependent compressed coil volume. The "hooking" of the coils occurring above a certain concentration are assumed by *Schurz* to lead to an infinitely extended network[12]. The dependence of the viscosity of the polymers upon their molecular weight ("Bueche-plot") can be used to determine the mesh width of this network[13]. *Schurz* therefore proposed replacement of the distinction between "dilute" and "concentrated" solutions of polymers by the more comprehensive one between "particle solutions" and "network solutions"[14].

A very important contribution to the question of the properties of polymer coils in highly concentrated solutions is due to *Vollmert* and *Stutz*[15]. They attempted to solve the problem by chemical means, with the aid of crosslinking reactions which proceed exclusively by intermolecular mechanisms. To this end a polymer containing the functional group x was mixed with a second polymer containing the functional group y. In this experiment x and y can react with each other quantitatively, but no reaction is possible between x and x or y and y. The concentration-dependent conversion, *i.e.* the consumption of functional groups during the reaction, and the proportion of crosslinked polymer formed will, under certain conditions, afford the degree of interpenetration of the coils.

These experiments were carried out with, *e.g.* a random copolymer of butyl acrylate with 2-isocyanatoethyl acrylate monomer units and a second random copolymer of butyl acrylate with 4-hydroxybutyl acrylate monomer units (Scheme 1). On mixing of the two previously separately dissolved polymers, the conversion displays a pronounced dependence upon the polymer concentration as expected; below 5 wt % conversion was very low and the resulting gel consisted merely of coils linked together only at the surface *via* urethane groups. Although the intermolecular reaction between the coils in the external regions steadily increases as the concentration of polymer rises, the reaction does not go to completion, thus indicating the coils to be largely impenetrable. On use of the polymer containing the same hydroxyl group with hexamethylene diisocyanate as reactant the reaction goes to completion because the low molecular crosslinking agent can penetrate unhindered into the interior of the coils.



Scheme 1

There are two principal objections to the postulated inability of coils to engage in mutual interpenetration: it is conceivable that a rapid reaction between individual functional groups occurring on mixing of the two dissolved polymers may lead to fixation of chain segments; this could stop the system reaching the end point of interpenetration corresponding to maximum entropy. Another argument is the general incompatibility of chemically different polymers; under the experimental conditions employed this could have led to a separation of the NCO- and OH-containing macromolecules and thus simulate an impression of impenetrability of the coils.

Vollmert attempted to counteract these misgivings by permitting reaction of polymers with different contents of functional groups and then extrapolating to any desired low values of functional groups; the chemical difference should then no longer be significant. Even under these conditions the maximum attainable conversion for 30 % polymer solutions is only about 16 to 18 % so that on exclusion of possible hindrance to reaction by crosslinking or incompatibility incomplete interpenetration still has to be assumed. According to this interpretation the reacted functional groups are located only in the outer or contact zones of the coils while the monomer units in the interior of the coils cannot react.

In order to further examine this concept, the reaction of a poly(methyl methacrylate) containing hydroxyl groups with an equivalent amount of a polymer having acyl chloride groups

[*] In a "theta solvent" a polymer solution displays pseudoideal behavior, which of course also depends upon temperature (so-called Θ temperature); $\Delta H_{mix} = \Theta \Delta S_{mix}$.

was investigated near the Θ state[*] in benzene/*n*-hexane mixtures. Approximately the same degree of coil interpenetration was found as in good solvents, *i.e.* 5 to 20% of the coil volume[16]. Hence it follows that the theory of excluded volume is not applicable to the problem of coil interpenetration and in spite of the absence of a thermodynamic hindrance, steric reasons must be responsible for the observed "cell structure" also at the Θ point[17].

Finally, a completely different concept of the morphology of macromolecular materials also deserves mention: *Schoon et al.*[18] regard the structure of such polymers in the dissolved and solid state as a kind of packing of approximately equal sized tertiary spheroids linked together by a common molecular thread. For each polymer the size of the tertiary units is assumed to be a kind of material constant. This picture has been derived mainly from electron microscope studies and from the results of ultrasonic degradation of polymers[19]; no support has yet been obtained from other physical or chemical experiments.

3. Recent Results

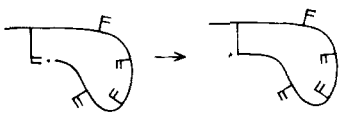
The findings discussed in Sections 1 and 2 show a distinct disagreement to exist between the classical ideas of the coil structure of dissolved and amorphous solid polymers with extensive interpenetration and the cell model supported in particular by the work of *Vollmert* in recent years. Further investigations will therefore have to shed fresh experimental and theoretical light, in order to permit a decision in favor of one of the opposing views or a modification of previous concepts. The present article is concerned mainly with "chemical probes" for examining molecular shape and will not give detailed consideration to any of the purely physical methods employed in recent years. Apart from crosslinking copolymerization, recent experiments on inter- and intramolecular chain linkage are discussed[20]. Among the physico-chemical methods, mention should be made of the use of spin-labeled macromolecules for the study of interactions between various polymers whose monomer units contain unpaired electrons; this technique is still in its infancy (cf., *e.g.*[21]) but holds promise of interesting information about chain mobility of macromolecules and their relaxation phenomena and also about chain conformations. Preliminary results obtained with concentrated poly(vinyl butyrate) solution in ethanol suggest shrinkage of the coils with increasing polymer concentration to below Θ dimensions[21].

3.1. Crosslinking Copolymerization

On copolymerization of a monovinyl compound with a nonconjugated divinyl monomer, the resulting macromolecules branch already after very small conversions since the divinyl compound is tetrafunctional owing to the presence of two reactive double bonds. An active growing chain terminus can therefore react not only with monomer molecules but also with "pendant" double bonds on previously formed "dead" macromolecules so that each unit of the divinyl monomer incorporated into a polymer chain is a potential crosslinking site.

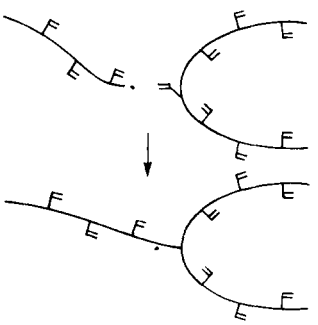
[*] See footnote on p. 452.

On extensive dilution, *i.e.* when the growing chains are largely present as isolated coils, there is a high probability that for a sufficient chain length the active chain end will react with a double bond on the same macromolecule, leading to intramolecular linkage, *i.e.* a cyclization point (Scheme 2).



Scheme 2

In contrast, intermolecular reactions are only possible if the growing chain is sufficiently close to another one, *i.e.* to another coil; this depends mainly on polymer concentration and thus also on the conversion attained in the polymerizing system. This reaction leads to braching sites (Scheme 3).



Scheme 3

Provided that it is possible to determine the ratio of intra- and intermolecular reactions as a function of the conversion, direct conclusions can then be drawn regarding the extent of coil interpenetration. However, a knowledge is required of the reactivity of the active chain ends and the related incorporation ratios of mono- and divinyl compounds into the growing chain, as is an experimental means of distinguishing between cyclization (Scheme 2) and branching reactions (Scheme 3).

3.1.1. Copolymerization Kinetics

Joint polymerization of two or more monoolefins, *e.g.* monovinyl compounds, can be quantitatively described under certain conditions by the known copolymerization equation. On this basis it is also possible to determine the composition of a copolymer from two or more different monomer units as a function of the monomer ratio and the conversion. The calculation becomes somewhat more complicated if a monoolefin (M_1) is copolymerized with a diolefin (M_2). Not only must the two monomers M_1 and M_2 be considered but also the pendant reactive double bond (M_3 from M_2) and the repeat units incorporated *via* the two double bonds (crosslinking sites N from M_2).

Several publications have been concerned with this problem from a kinetic standpoint[22-26]. In contrast to a normal binary copolymerization of two monoolefins with four possible growth steps, crosslinking copolymerization requires consideration of nine growth reactions. Under certain conditions, however, the calculations can be greatly simplified[26]: the double

bonds of the monomeric diolefin M_2 must possess the same polymerization activity as the double bonds M_3 attached to existing polymer chains which have arisen from the same diolefin already polymerized *via* one double bond. Of course, this only applies if the two double bonds are independent of each other and are not conjugated or in resonance, as *e.g.* in *m*-divinylbenzene, and if the diolefin cannot undergo cyclopolymerization. Under these conditions the change in concentration of the monomers, the attached double bonds, and the crosslinking sites can be described in terms of the degree of polymerization by a series of differential equations which can be solved by stepwise integration provided that the copolymerization reactivity ratios are known[26].

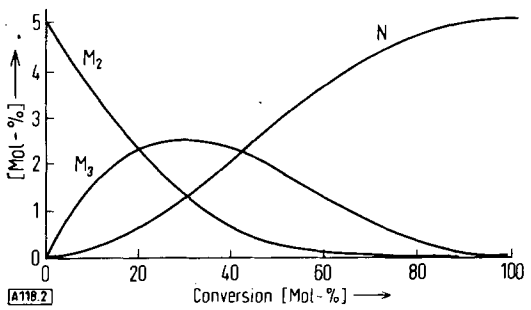
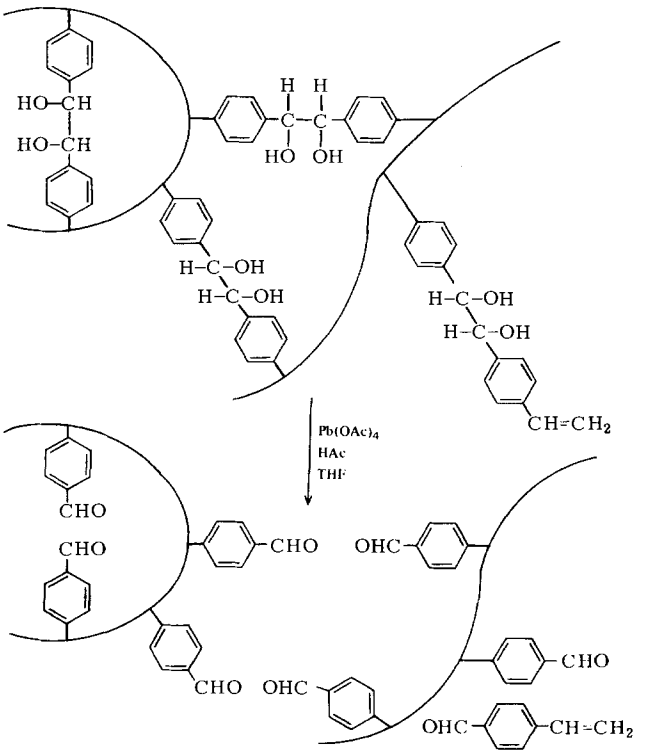


Fig. 2. Copolymerization of ethylene dimethacrylate (EDMA) and styrene. Concentration profile of EDMA (M_2), attached double bonds (M_3), and crosslinking sites (N) as function of conversion for an initial 5 mol % concentration of EDMA.

As an example, Figure 2 shows the results obtained for the copolymerization of ethylene dimethacrylate (EDMA) and styrene for 5 mol % of EDMA in the starting mixture. The concentration of the diolefin (M_2, EDMA) initially decreases rapidly, then more slowly until M_2 is completely incorporated into the polymer chain at *ca.* 90 % conversion. Accordingly, the concentration of attached double bonds (M_3) initially increases, reaching a maximum at 30 mol % and then decreases because reaction of these double bonds forms additional crosslinking points (N) which attain the initial concentration of the diolefin at quantitative conversion. Similar situations, dictated by the copolymerization reactivity ratios and the chosen monomer ratios, are observed in other systems[26]. They provide a basis for the following views on the competition between inter- and intramolecular growth steps of crosslinking polyreactions.

3.1.2. Polymers Having Cleavable Network Bridges

A distinction between inter- and intramolecular crosslinking can be accomplished with polymers made up of diolefins which can be cleaved by simple and chemically unequivocal methods after their introduction into a macromolecule. Any opening of intramolecular bonds, *i.e.* rings, in the process will not affect the molecular weight of the polymer, whereas a decrease in molecular weight will occur in the case of splitting intermolecular crosslinks. There are several divinyl compounds which are suitable for such studies. Thus monomers having benzyloxycarbonyl groups[22], which can be cleaved with hydrogen bromide and glacial acetic acid, azomethine groups which are ruptured by acid treatment[23,27], and ethylene glycol groups which can be scissioned by lead tetraacetate[28] have all been used. Scheme 4 illustrates the cleavage of products arising from *e.g.* styrene and 1,2-bis(4-vinylphenyl)-1,2-ethanediol (DSG).



Scheme 4

The crosslinks are opened to form *p*-vinylbenzaldehyde monomer units which can be determined, *e.g.*, by IR spectroscopy[28]. Since determination of the molecular weight of crosslinked, and hence insoluble polymers, is impossible, polymerization must be broken off shortly before the gel point; the

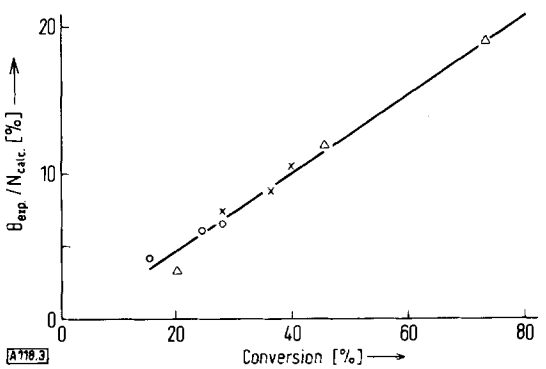


Fig. 3. Ratio of experimentally determined branching sites (B) to the calculated total number of all linkage sites (*i.e.* the sum of branching and cyclization sites) as a function of conversion in the radical copolymerization of 1,2-bis(4-vinylphenyl)-1,2-ethanediol (DSG) and styrene. Initial total monomer concentration 2 mol/l. o, 5 mol %; Δ, 3 mol %, ×, 1 mol % DSG at commencement.

(branched) polymers are then cleaved and the molecular weights recorded before and after cleavage are compared. The experimentally determined number of branching sites

can then be correlated with the total number of crosslinking sites, *i. e.* the sum of the branching and cyclization sites, which can only be computed as an overall sum.

Figure 3 shows the results obtained for copolymers of DSG and styrene. Within a relatively broad range of composition of the starting mixture (between 1 and 5 mol % DSG) the ratio of the experimentally determined branching sites to the sum of the calculated branching and cyclization sites for a given concentration of starting monomer depends practically only upon the conversion. The considerable difference between experiment and calculation demonstrates that in the system investigated up to 20-fold fewer branching sites are formed than were expected. This would indicate that, even for relatively high conversions, *i. e.* in this case high polymer concentrations, there is an unexpectedly large number of cyclization steps during the polymerization, which can only be explained by pronounced hindrance of the access of growing macromolecules to the double bonds attached to other coils. Thus crosslinking copolymerization proves to be an example of strongly hindered coil interpenetration; this finding has considerable consequences for the network structure of the polymers, which is certainly highly inhomogeneous in the case discussed.

However, it must be clearly emphasized that the modest interpenetration found for crosslinking polymerization should not be generalized and applied to linear polymers, for network formation will undoubtedly lead to some shielding of the attached double bonds in the coil interior against approaching polymer chains so that they will react primarily in the boundary regions of the coils.

A deficit of this magnitude between predicted and calculated crosslinking yields as a result of preferential intramolecular cyclization or sterically conditioned incomplete reaction of attached double bonds has repeatedly been observed[22,23,29-32]. The extent of cyclization or of unconsumed attached double bonds is distinctly dependent upon the nature of the tetrafunctional comonomer M_2 and upon the reaction conditions. While it must be assumed at the onset of reaction that chain initiation can occur practically anywhere in the system owing to the high concentration of monomer, the proportion of monomer will fall with increasing conversion, *i.e.* with increasing polymer content; nevertheless, a growing chain is much more likely to encounter a monomer molecule than an unconsumed attached double bond at not too high concentrations of crosslinking agent, *i.e.* $[M_2] \ll [M_1]$, and of course also at very high conversions. Moreover, the proven high degree of cyclization also demonstrates that an intramolecular reaction of the growing chain end with an attached double bond of the same macromolecule occurs much more frequently than intermolecular linkage of different macromolecules. The consequence is the above-mentioned inhomogeneity of the network in which the average inter-crosslink distance and the length of the network chains cannot be calculated solely from the content of crosslinking agent. Thus the "stoichiometric crosslink density" is not only determined by the true intermolecular network bridges and the chain entangling physically effective mainly in the boundary regions of the coils occurring on hindered interpenetration, but must be corrected for the proportion of crosslinking agent "lost" by cyclization, as already pointed out by *Wesslau*[32]. The importance of these findings for the pore structure in polymeric networks, *e.g.* for gel permeation chromatography, and for crosslinking polycondensation can only be mentioned in passing.

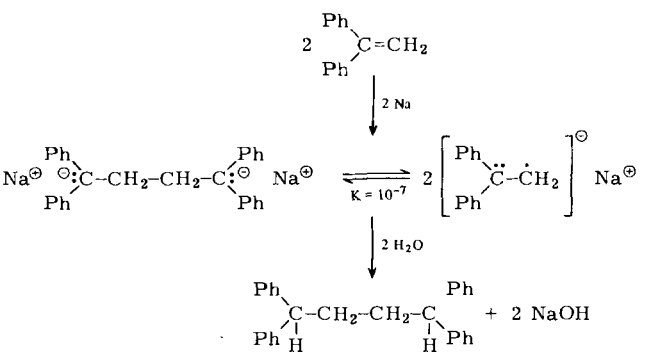
3.2. Reactions of Macromolecules

3.2.1. Polyradical Ions

Low-molecular substances can usually react in high yields with macromolecules bearing functional groups in homogeneous solution; for instance, the polyacrylates containing hydroxyl groups which were used by *Vollmert* undergo over 90 % complete reaction with hexamethylene diisocyanate in the entire accessible range of polymer concentration between about 0 and almost 100 wt %[15]. Again, intermolecular linkage leads to crosslinking and gel formation, while rings are formed by intramolecular reaction. Since the two possibilities cannot be distinguished experimentally, such experiments provide no information about interpenetration of the coils.

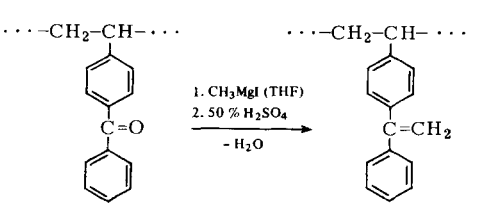
A different situation arises, however, if the polymer contains only one sort of functional groups which can react with each other and thus obviate the need for a low-molecular co-reactant. The question of incompatibility of the reacting polymer chains then also becomes irrelevant because only chemically similar macromolecules are present in the system. However, the functional groups may only be generated on the polymer immediately prior to the intended linking reaction since it will hardly be possible to control the reactions of a polymer whose functional groups can react with each other.

A number of polymeric radical ions are found to be suitable for such purposes. It has long been known that reaction of 1,1-diphenylethylene with sodium rapidly and unequivocally affords radical anions which undergo immediate and practically quantitative dimerization (Scheme 5)[33-35].



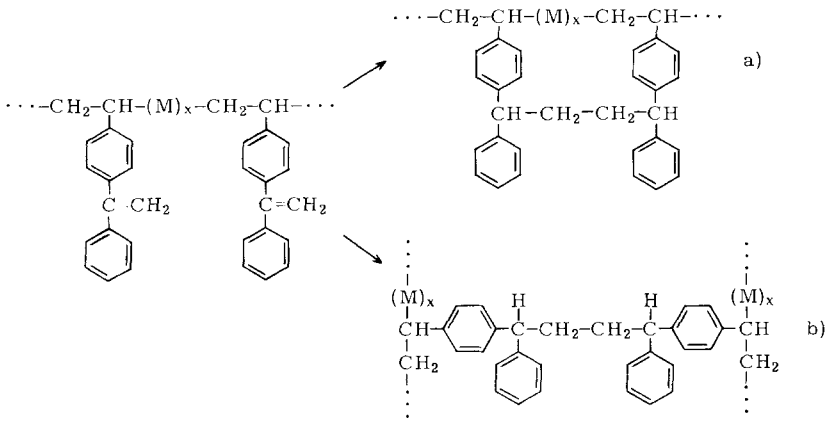
Scheme 5

Polymers containing 1-phenyl-1-(4-vinylphenyl)ethylene monomer units were subjected to analogous reaction with naphthalenesodium. The starting polymers cannot be obtained by polymerization of 1-phenyl-1-(4-vinylphenyl)ethylene, which reacts in a rather obscure manner owing to its two double bonds, but is available by a polymer analogous reaction from 4-vinylbenzophenone/styrene copolymers (Scheme 6)[36,37].



Scheme 6

In these macromolecules the content of functional groups and their mutual separation along the polymer chain can be varied within wide limits. If the reaction with naphthalene-sodium is performed at high polymer dilution and low functional group content, intramolecular linkage will predominate and coil contraction will therefore occur, as is manifested in a decrease in intrinsic viscosity (Scheme 7, cf. Table 1)[38].



Scheme 7. a) Intramolecular reaction; dilute solution, x is small. b) Intermolecular reaction; concentrated solution, x is large.

At very low polymer concentrations the coils are apparently far enough apart to preclude contact or interpenetration. If, under the same concentration conditions, more functional groups are introduced into the polymer and subjected to intramolecular reaction, then relatively small rings will be formed on the macromolecules; as in ladder polymers these rings lead to stiffening of the chain, *i.e.* to an increase in the intrinsic viscosity. However, if the polymer concentration is raised in the reaction, recognizable gel formation occurs above about 2.5 wt %; this is therefore the "critical" concentration above which contact occurs between different coils and intermolecular reaction becomes possible. In a 5 % solution of a polymer with 1 mol % of functional groups about 40 wt % of the polymer will undergo crosslinking; at the same concentration and 5 mol % of functional groups considerably more than 90 % of the coils are linked intermolecularly. Bearing in mind that in the reaction of polymers containing hydroxyl and isocyanate groups described by *Vollmert* only about 2.5 % of all groups had reacted at a polymer concentration of 10 wt % and 5 mol % of functional groups, it follows that in the present case of a chemically homogeneous polymer considerable coil interpenetration must have occurred since the extent of crosslinking would otherwise have been much lower. Since no macromolecular incompatibility is to be expected in the solutions used for generating polyradical ions, the system studied can be viewed as demonstrating that individual coils are not necessarily present above the critical polymer concentration. The reacting polymer chains are subject to at least very extensive interpenetration and thus behave in a fundamentally different manner from the previously described mixtures of chemically different macromolecules in which coil separation occurs for thermodynamic and possibly also for steric reasons.

Table 1. Intrinsic viscosities of styrene/1-phenyl-1-(4-vinylphenyl)ethylene (PVDE) copolymers before and after reaction with naphthalenesodium.

Polymer concentration	pVDE in copolymer [mol-%]	[η] [ml/g] [a] before reaction	after
Particle solution			
0.5 wt %	0.5	83	67
1 wt %	1.0	78	77
	2.0	81	91
	5.0	83	100
Network solution			
2.5 wt %	0.5	83	92
	1.0	78	104
	2.0	81	127

[a] In benzene at 20 °C.

3.2.2. Purely Intramolecular Reactions

In connection with the occurrence of cyclization on reaction of dissolved macromolecules with low-molecular reactants, the limiting case of purely intramolecular reaction warrants special attention. Theoretical calculations have long been available which describe the change in solvent viscosity of a polymer as a function of the number of linkages and of ring size[39].

A linear macromolecule consists of N_m statistical chain segments which in turn contain s_m monomer units. For the overall molecule having a degree of polymerization P, then:

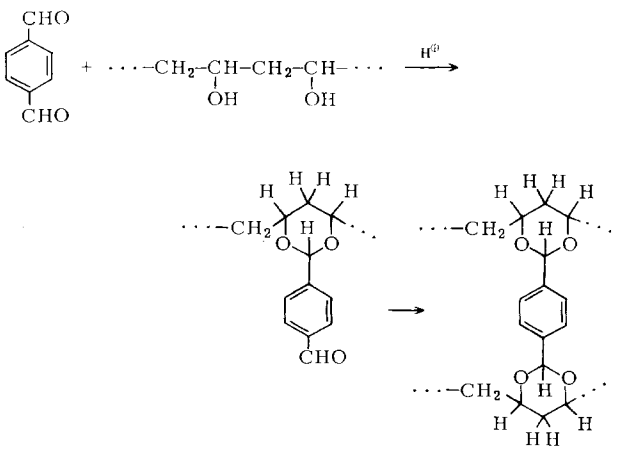
$$P = N_m \cdot s_m$$

If each monomer unit contains one functional group, which can all suitably be linked together (examples, *vide infra*) by a functional reagent, then at very small polymer concentrations a purely intramolecular reaction will occur leading to a greater or lesser number of rings in the chain depending upon the number of linkage sites. *Kuhn* and *Majer*[39] were able to show that the probability of formation of a k-membered ring rapidly decreases with increasing k, and when $k = 50$ is only *ca.* 1‰; the effect of chain length above $N_m = 10^2$ plays a very minor role. Thus mainly small rings are formed within a macromolecule; in this way the coil dimensions are reduced relative to those in the original linear molecule prior to ring formation. In the case of practical interest with only few

cyclizations per macromolecule, *i.e.* small values of ν, it can be shown that the intrinsic viscosity $[\eta]$ of the purely intramolecularly linked polymer is related to that of the starting material $[\eta]_0$ by the following equation:

$$[\eta]=[\eta]_0\left(1-\nu\sqrt{\frac{2}{N_m}}\right)$$

Since, for a given degree of polymerization and known length (s_m) of the statistical chain segment N_m, this equation contains only the number of linkage sites ν and the readily determinable solvent viscosity, its validity can easily be tested, provided that a system is chosen whose linkage reaction proceeds unambiguously even at high dilution. In the preliminary experiments of *Kuhn* and *Balmer*[40], poly(vinyl alcohol) of molecular weight 100000 was allowed to react with terephthalic aldehyde at various polymer concentrations in water, to form acetals (Scheme 8).



Scheme 8

Subsequent detailed investigations[41] on poly(vinyl alcohols) of various chain lengths showed excellent agreement between the calculated and experimental decrease in intrinsic viscosity. Figure 4 shows the change in $[\eta]$ for a poly(vinyl alcohol) of average molecular weight 14200 under various experimental conditions. The condition of low linkage site number stipulated in the derivation of the above equation is satisfied (the range of one molecule of terephthalic aldehyde to 0.4 to 2 macromolecules, *i.e.* to 200 to 2500 monomer units of vinyl alcohol or OH groups). As shown, the viscosity decreases after the reaction for polymer concentrations up to 0.5 wt %, which is not due to chain degradation but to the above-mentioned coil contraction. In reactions above this concentration the intrinsic viscosity rises above that of the starting poly(vinyl alcohol) since the close spatial proximity of the coils leads to intermolecular linkages; up to about 1.5 wt % polymer concentration the molecular weight of the polymer increases two- to three-fold, without gel formation because only few coils are initially linked and a true network has not yet formed. In this system it can therefore be precisely demonstrated that purely intramolecular ring formation only occurs at very low polymer concentrations; in this case the critical concentration of incipient coil contact can be accurately determined without having to resort to the difficultly quantifiable phenomenon of "gel formation". In the purely intramolecular range at 0.1 wt % polymer concentration, the intrinsic viscosity displays a very good agreement between theory and experiment (Fig. 5); the calculations of *Kuhn* and *Majer*[39] are thus confirmed in excellent manner.

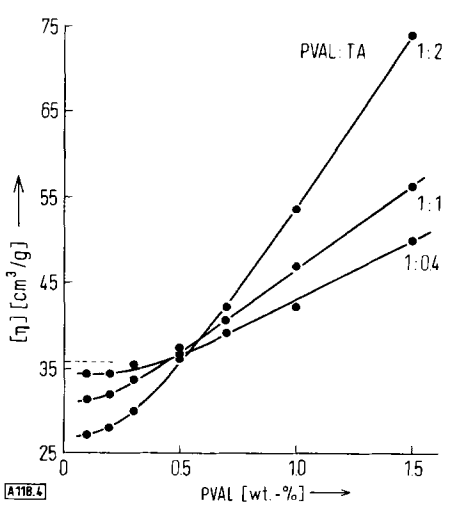


Fig. 4. Intrinsic viscosity (measured at 25 °C in water) after reaction of poly(vinyl alcohol) (PVAL, molecular weight 14200) with terephthalic aldehyde (TA) in 0.1 N HCl at various polymer concentrations and molar ratios (PVAL:TA) of the reactants. ------, intrinsic viscosity of poly(vinyl alcohol).

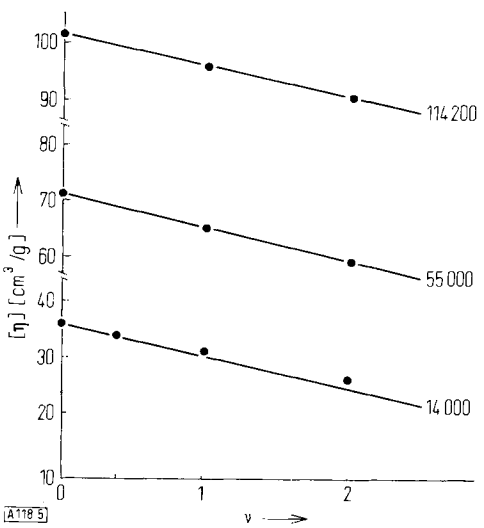
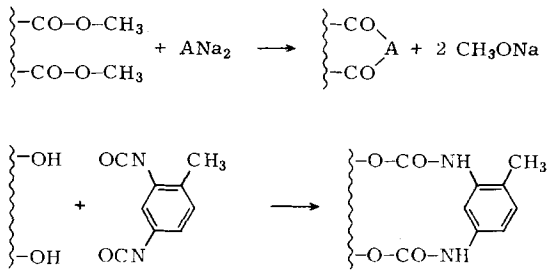


Fig. 5. Intrinsic viscosity (in water at 25 °C) of poly(vinyl alcohols) (PVAL) after reaction with terephthaldehyde (TA) as function of the number of crosslinks ν per macromolecule (reactions with 0.1 wt % polymer concentration in 0.1 N HCl). The number average molecular weight $\bar{M}_n$ is noted alongside the curves. Solid curves calculated, dots experimental.

This limiting case of a purely intramolecular reaction will certainly prove applicable to other systems, although hardly any experimental information has yet been published. A significant decrease in intrinsic viscosity was also observed in the purely intramolecular reaction of copolymers of styrene and methyl acrylate with 9,10-dihydroanthracenedisodium (ANa_2) and of styrene/vinyl alcohol copolymers with 2,4-toluylene diisocyanate (Scheme 9)[42].

Similar studies are also available on the reaction of partially esterified poly(vinyl alcohols) with aliphatic and aromatic diacyl chlorides in dilute solution, in which an—albeit relatively slight—decrease in limiting viscosity was likewise observed[43].



Scheme 9

Suitable objects for study would be, *e.g.* complex formation between polymers containing salicylic acid and iron ions[44], as well as reactions of polyacrylic acid solutions and 2,2'-dichloro-*N*-methyldiethylamine as crosslinking agent[39] or of rubber in benzene with suitable vulcanizing agents. Comparison of theory and experiment should also permit conclusions regarding the extent of random or nonrandom ring closures.

4. Conclusion

As is apparent from the investigations described, the present state of the art does not permit a general answer to the question of interpenetration of macromolecular coils. In crosslinking polyreactions and reactions between chemically nonidentical macromolecules in solution, penetration is hindered and generally only slight. In principle, in such cases the true situation is well represented by *Vollmert*'s cell model. The conclusions regarding the structure of crosslinked polymers are of considerable importance. Not only the long-predicted inhomogeneity of networks formed from copolymerizing vinyl- and divinyl compounds at various copolymerization reactivity ratios[45], but also the reactions involved in industrial curing and vulcanization processes have been inadequately investigated with respect to the incompleteness of molecular interpenetration. Particular interest is commanded by studies on the use of defined structural segments for construction of crosslinked polymers; most suited are polyaddition reactions leading to polyurethanes or crosslinked epoxy resins. With the aid of such purpose-built networks, relationships between the structure of chain-linking segments and physical properties of polymers become amenable to study, as described by *Batzer, Lohse,* and *Schmid*[46] in the field of epoxy resins. Formation of only poorly interpenetrating macromolecules is also to be expected in noncrosslinking polycondensation since high molecular weights are then attained only on very high conversions; in the later stages of the reaction, however, hardly any monomer molecules are available and the polymer chains already formed are constrained to react with each other *via* their end groups. Relevant model studies in highly concentrated solutions or melts have yet to be performed.

In contrast to the above cases of hindered coil interpenetration in crosslinking polyreactions and in systems of chemically nonidentical macromolecules, available evidence pertaining to reactions of chemically uniform macromolecules in thermodynamically good solvents clearly suggests pronounced coil interpenetration. In the limiting case of very high dilution, viscosimetric measurements unequivocally demonstrate the intramolecular cyclization reactions exclusively possible far below the critical polymer concentration and provide a theoretical basis for their understanding. The region of incipient coil contact in dilute polymer solution can also be recognized. Little attention has so far been devoted to the effect of solvent quality on coil interpenetration. The practical significance of this problem also deserves mention: on film formation from thermodynamically good solvents, evaporation of the solvent will lead to very dense films; however, if largely nonpenetrating polymer coils are present in thermodynamically poor solvents, a film having a loose porous structure must be expected on solvent evaporation[47]. Phase separation may even occur in mixtures of thermodynamically good and poor solvents of differing volatilities—the resulting systems display macromorphological structures and have found industrial application, *e.g.* as bubble coatings[48]. These are films having a cavity structure resulting from phase separation on drying of the solutions. Owing to the differing refractive indices between film former and air in the bubbles, white coatings of good hiding power are obtained without use of white pigments.

Present-day concepts regarding the problem of coil interpenetration in dissolved and amorphous solid polymers can therefore be summarized thus: Largely noninterpenetrating systems are known which can be adequately described by *Vollmert*'s cell model, as are polymers in which there is very distinct interpenetration of individual coils in keeping with the theory of *Flory*. Even in the latter case, no generalization is yet permissible since neither the influence of solvent quality nor the effect of the "stiffness" of the polymer chain have been studied in detail, and previous work has been mainly concerned with flexible vinyl polymers.

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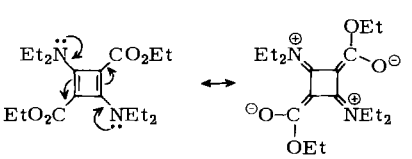
Vinamidines and Vinamidinium Salts—Examples of Stabilized Push-Pull Alkenes

By Douglas Lloyd and Hamish McNab[*]

The name vinamidines has been proposed for 1,5-diazapentadienes; these compounds can be regarded as vinylogous amidines and at the same time as push-pull substituted (and thereby stabilized) alkenes. Vinamidine and vinamidinium structural elements may also form part of a ring system. Characteristic of this class of compounds are their reactivity toward electrophiles (at C_β) and nucleophiles (C_α) and their regenerative character, *i.e.* their tendency to undergo substitution instead of addition reactions. Reactions of vinamidinium salts with nucleophiles are of special preparative value: they lead *e.g.* to pyrazoles, oxazoles, pyrimidines, diazepines, quinolines, and quinolizines.

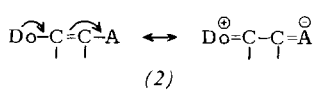
1. Introduction—'Push-Pull' Alkenes and Their General Properties

The 'push-pull' concept has in recent years received some attention because of the way it has been used to provide extra stability to otherwise unstable systems. Perhaps the most obvious example has been its use in providing stable compounds which formally possess a cyclobutadiene ring, *e.g.* *(1a)*[1]. This is stabilized by a push-pull effect between the electron-donating amino groups and the electron-withdrawing ester groups. Thus, in resonance terminology it is possible to write a further contributing form which is dipolar *(1b)*.



(1a) *(1b)*

Any push-pull alkene has an electron-donating group (Do) attached to one end of a double-bond and an electron-withdrawing group (A) to the other end, and these groups interact with each other as illustrated in *(2)*.



(2)

When electron-donor or electron-acceptor groups are separately attached to alkenes they give rise to, respectively, electron-rich and electron-poor double-bonds, and this results in such alkenes having characteristic properties, *e.g.* the nucleophilic character of enamines, and the electrophilic character of α,β-enones, as shown, for example, by their participation in Michael reactions.

What happens when both electron-donor and electron-acceptor bonds are attached to an alkene group? Depending upon the reaction partner the molecules behave as nucleophiles or as electrophiles. This is nicely exemplified by the reactions of the push-pull cyclobutadiene *(1)*[2].

Another property of push-pull alkenes is their enhanced stability, due to delocalization of electrons from the donor group through the double bond to the acceptor group. This stability leads to such molecules having a tendency to undergo substitution reactions rather than the addition reactions characteristic of most alkenes. For example, in the case of electrophilic attack on push-pull alkenes, loss of a proton from

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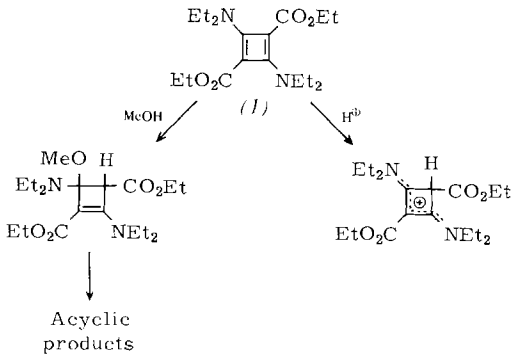
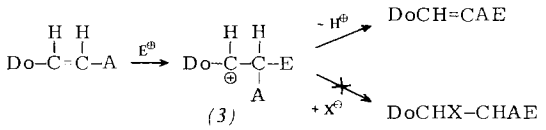
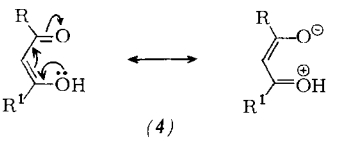


the positively charged intermediate *(3)* tends to take place rather than addition of an anion, because the fundamental stability of the push-pull alkene system is thereby regenerated.



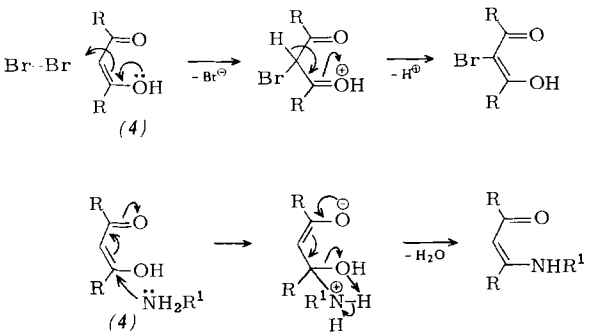
Thus, to summarize, push-pull alkenes are characterized by their reactivity towards both electrophiles and nucleophiles, and by their enhanced stability, which makes them prone to substitution rather than to addition reactions. The compounds thus show meneidic or regenerative character[3], and are also relatively easy compounds to handle. For these reasons they are also suitable reagents for a variety of syntheses.

Probably the first push-pull alkenes to be investigated were the β-diketones *(4)* and their metal derivatives.



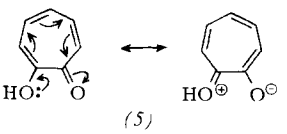
It was at one time thought that in the metal derivatives there was complete cyclic delocalization of electrons involving both the diketone moiety and the metal atom[4], but the present interpretation regards the delocalization as being confined to the diketone part of the molecule[5].

β-Diketones *(4)* provide excellent examples of the reactivity of such systems towards electrophiles and nucleophiles and also of their meneidic character.

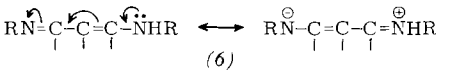


Tropolones *(5)* are vinylogs of β-diketones and their stability and characteristic reactivity are ascribable to their being push-pull alkenes[6].

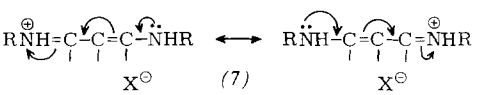
Hence they readily undergo both electrophilic and nucleophilic substitution. This picture of the structure and reactivity of tropolones is in accord with the results of X-ray structure determinations, which show the C(1)—C(2) bond to be effectively single and little involved in the conjugation.



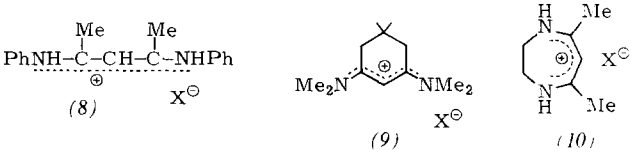
In the examples considered hitherto a carbonyl group always acts as the electron-acceptor group. An imino group can likewise take over this function. If the electron-donor group is an amino group we then have the push-pull alkene system *(6)*.



This has been called a vinamidine system because it represents a vinylog of an amidine[7]. Even more interesting are the vinamidinium salts *(7)*, because they can be symmetrical systems and are therefore particularly stable: The illustrated



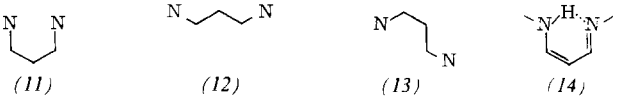
canonical forms are indeed identical and can be likened to Kekulé forms for benzene. Vinamidine and vinamidinium salts may be open-chain or included in ring systems.



Examples of vinamidinium salts are the compounds *(8)* and *(9)*, and the dihydrodiazepinium salts *(10)*. Some of the properties of such systems will now be considered.

2. Shape and Structure of Vinamidines and Vinamidinium Salts

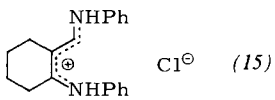
The vinamidine system may take up one of three distinctive shapes: all-*cis* ('U') *(11)*, all-*trans* ('W') *(12)*, and *cis-trans* ('sickle') *(13)*.



Open-chain vinamidines having an NH-group exist predominantly in the U-form[8–10], wherein they are stabilized by intramolecular hydrogen bonding *(14)*. The possibility that these bases possess a non-classical cyclic delocalized system of π-electrons involving the N—H bonds[11] has been ruled out[12]; they are indeed hydrogen-bonded vinamidines.

In contrast, their salts take up the W-configuration. This is shown quite unambiguously by the large vicinal coupling constants in their ^{1}H-NMR spectra[10,13].

In the case of cyclic vinamidines their configuration is forced upon them by the shapes of the rings in which they are incorporated. Thus dihydrodiazepines [cf. *(10)*] must have a U-form and derivatives of 3-imino-1-cyclohexenylamine [cf. *(9)*] must have a W-form, while the cyclohexene derivative *(15)*[14] probably has a sickle-form.

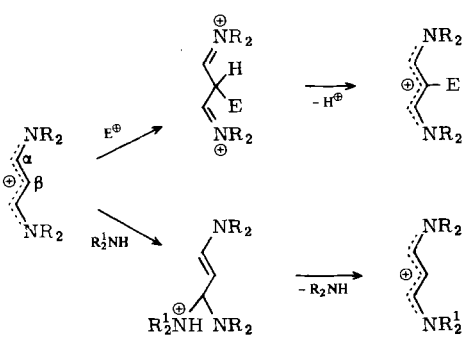


(15)

Within the chains of each of these forms the electrons are completely delocalized. This is clearly shown by the vicinal coupling constants in the ^{1}H-NMR spectra[15,16], and has been confirmed in the case of dihydrodiazepinium salts by X-ray structure determination[17]. There is an alternation of electron density along the systems, the terminal nitrogen atoms bearing the greatest density, while the α- and β-carbon atoms are relatively electron-poor and electron-rich, respectively. This is clearly shown by their ^{13}C-NMR spectra[17a]. Calculations which have been made on the vinamidine system are in accord with this data[18].

3. Reactions of Vinamidines and Vinamidinium Salts

Because of the alternating electron density in vinamidines and vinamidinium salts their α- and β-carbon atoms are, respectively, electrophilic and nucleophilic. Furthermore, attacks by nucleophiles and electrophiles, respectively, at these positions provide intermediate σ-complexes which can then lose a suitable fragment to give substitution products. These reactions proceed as shown in Scheme 1.



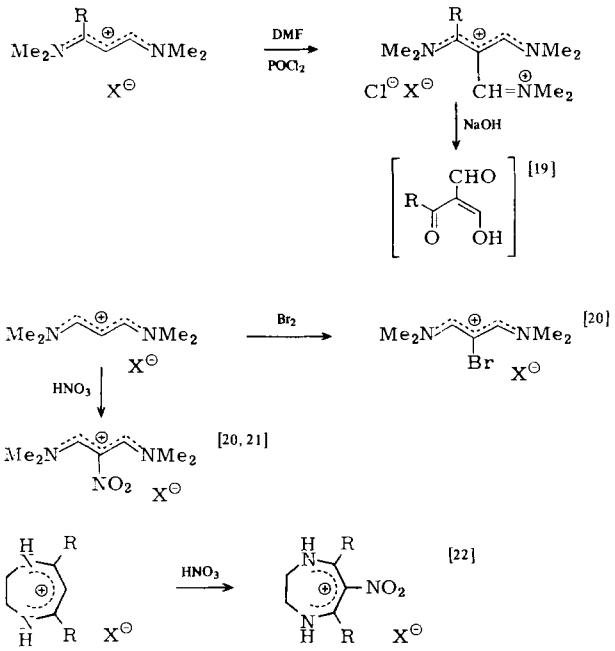
Scheme 1

The latter type of reaction has been of particular utility. Some examples of both types will now be given.

3.1. Reactions with Electrophiles

Both cyclic and acyclic vinamidinium salts react with electrophiles to give β-substituted products. The apparent anomaly that this involves electrophilic attack by one cation on another cation is easily understood when it is realized that vinamidinium ions are examples of electron-rich cations, having six electrons shared over five sites. Examples of such reactions are shown in Scheme 2[19–22].

While the commonest use of this reactivity has been to provide suitable substituted vinamidinium salts, it can also be used for more general purposes, as shown in the first

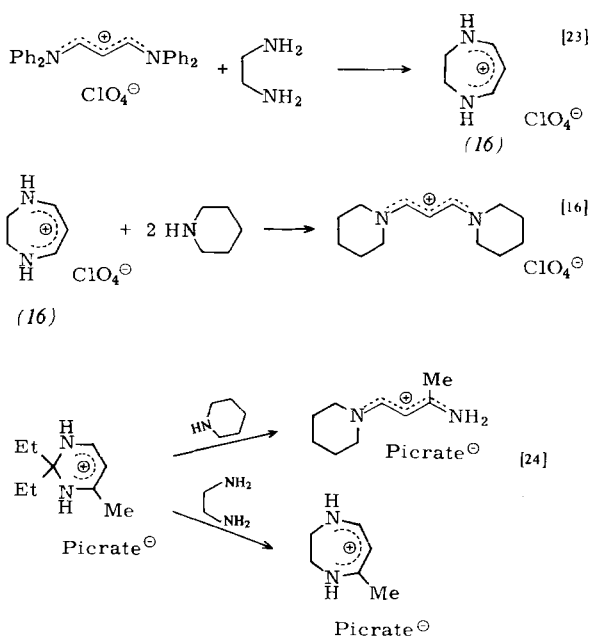


Scheme 2

example, where the reaction ultimately provided a method for the preparation of tricarbonyl compounds.

3.2. Reactions with Nucleophiles

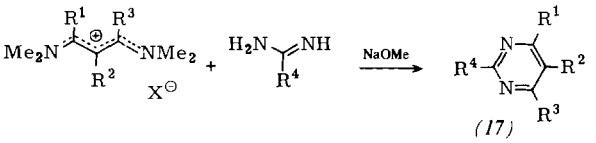
The reactions of vinamidinium salts with nucleophiles have almost all been carried out in order to prepare other types of compounds; sometimes when nitrogen nucleophiles are used the products are themselves examples of different types of vinamidines. Examples are depicted in Scheme 3[16,23,24].



Scheme 3

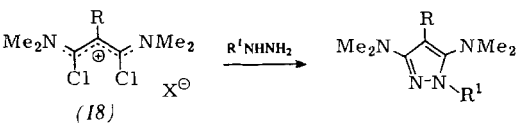
The first of these reactions provides a very convenient and valuable method for the preparation of dihydrodiazepinium salts; indeed the parent salt *(16)* is presently only obtainable in satisfactory yield by such a method[23].

Reaction of vinamidinium salts with amidines[25,26], guanidine[25-27] or thioureas[25-27] leads to a similar displacement of the terminal amino groups to give cyclic products, which in this case are not vinamidinium salts, but pyrimidines such as *(17)*.



(17)

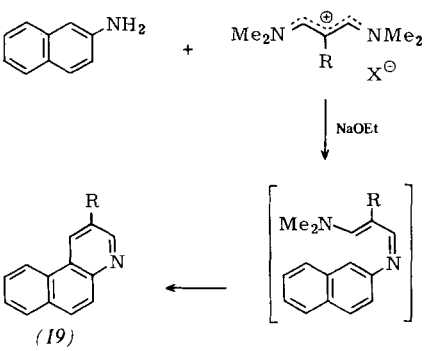
With suitably α-substituted vinamidinium salts, these substituent groups, instead of the terminal amino groups, may be displaced by the attacking nucleophile. Thus α,α'-dichlorovinamidinium salts *(18)* react with hydrazines to give bis(dimethylamino)pyrazoles[28,29].



(18)

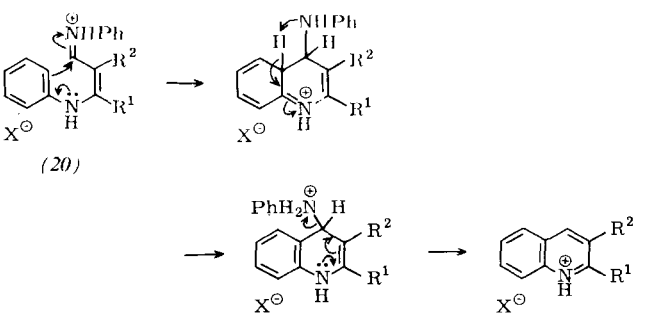
The salts *(18)* react in similar fashion with hydroxylammonium chloride, benzamidine, and *o*-phenylenediamine to give, respectively, bis(dimethylamino)-oxazoles, -pyrimidines, and -benzodiazepines[28].

β-Naphthylamine reacts with vinamidinium salts to give an intermediate which subsequently undergoes intramolecular cyclization to 4-azaphenanthrene derivatives *(19)*[30].



(19)

Some vinamidinium salts are capable of undergoing intramolecular cyclization. For example *N,N'*-diphenylvinamidinium salts *(20)* undergo cyclization with formation of quinoline derivatives when they are heated in acetic acid or in

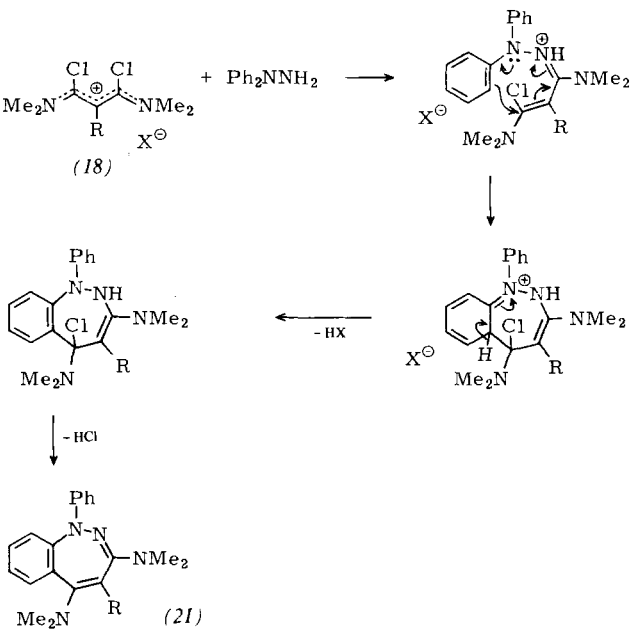


(20)

alcohols of similar boiling point[14]. This provides a very useful method for the synthesis of 2,3- and 1,2,3-substituted quinoline derivatives. Reaction presumably proceeds by the following mechanism[14].

Quinolines have also been prepared from vinamidinium salts by treatment of the latter with concentrated sulfuric acid[30a] or with aluminum chloride[30b].

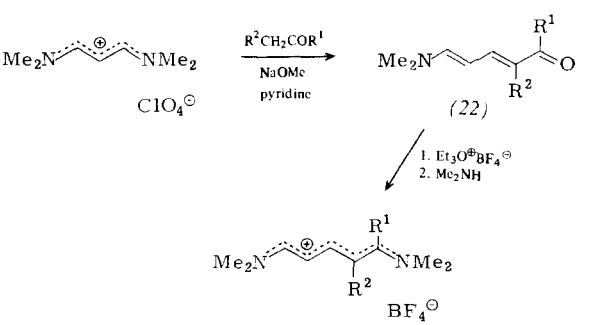
A further example of nitrogen nucleophilic attack on a vinamidinium salt which is followed by intramolecular cyclization is provided by the reaction of *(18)* with *N,N*-diphenylhydrazine to give a 1,2-benzodiazepine *(21)*[28]. Cyclization could involve a process related to that involved in quinoline formation.



(18) *(21)*

Carbon nucleophiles react with vinamidinium salts in an analogous fashion to nitrogen nucleophiles. The carbon nucleophiles are provided by suitable C—H acids in the presence of base; hence a variety of useful syntheses have been performed.

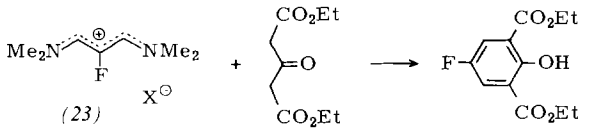
The carbanions derived from α-methyleneketones displace one of the amino groups of vinamidinium salts to give δ-aminopentadienones *(22)*[31], which can be further converted into



(22)

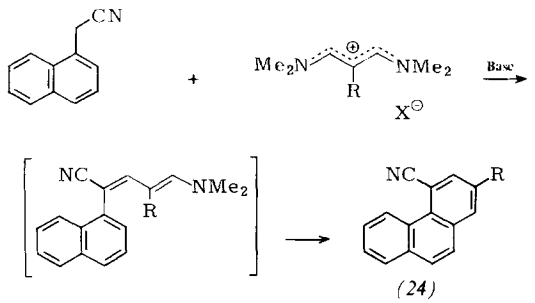
vinylogs of the vinamidinium salts. On reaction of the vinamidinium salt *(23)* with acetonedicarboxylic ester both amino groups are displaced and a phenol is produced[32].

A variety of ring-systems has been prepared by the interaction between vinamidinium salts and the carbanions derived from a number of substituted acetonitriles, RCH_2CN. The

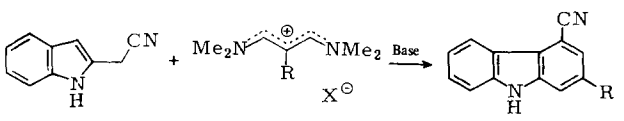


(23)

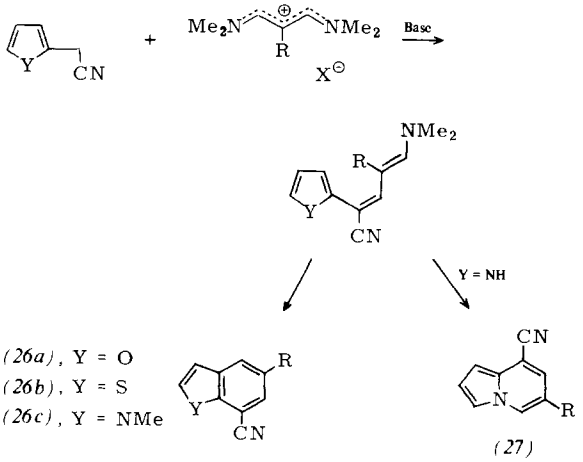
following examples show how this method has been utilized to obtain phenanthrenes (24)[30], carbazoles (25)[30], benzofurans (26a)[33], benzothiophenes (26b)[33], indoles (26c)[33], quinolizines (27)[33], and benzobiphenylenes (28)[34].



(24)

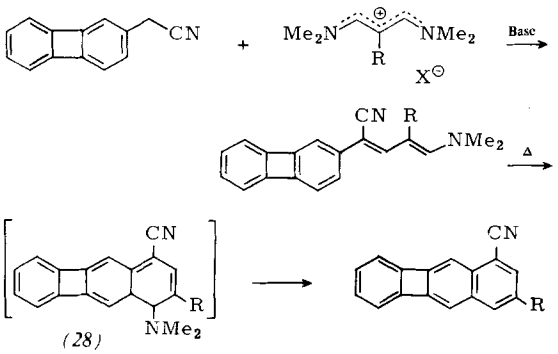


(25)



(26a), Y = O
(26b), Y = S
(26c), Y = NMe

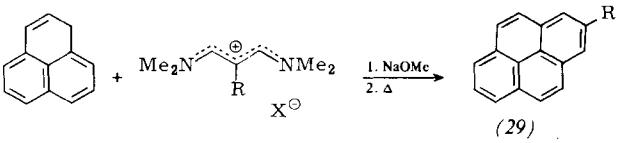
(27)



(28)

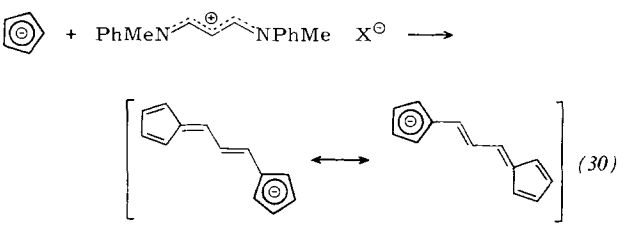
All of these reactions thus consist of initial displacement of one amino group of the vinamidinium salt by the carbanion, with subsequent loss of the second amino group in an intramolecular cyclization reaction.

A number of similar synthetic procedures involving other types of C—H acids have also been reported. Thus pyrenes (29) have been prepared by reactions of vinamidinium salts with phenalene[21, 30, 35, 36].

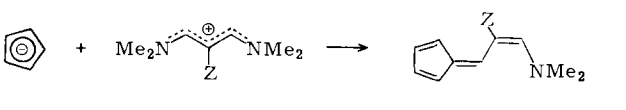


(29)

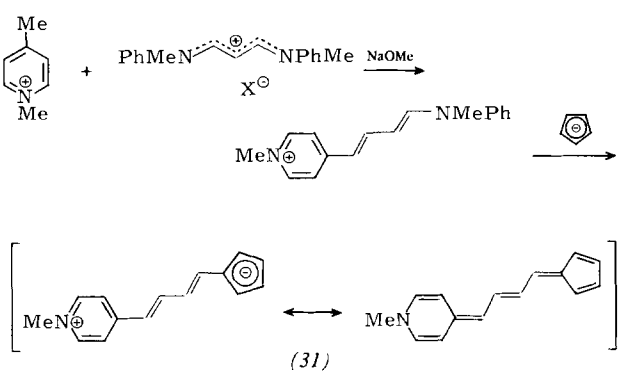
By reaction of a vinamidinium salt with the cyclopentadienide ion the interesting anion (30) was obtained[37]. Indene and fluorene analogs were also prepared[37, 38]. The cyclopentadienide ion has also been used for the preparation of 6-(dimethylaminovinyl)fulvenes[32].



(30)

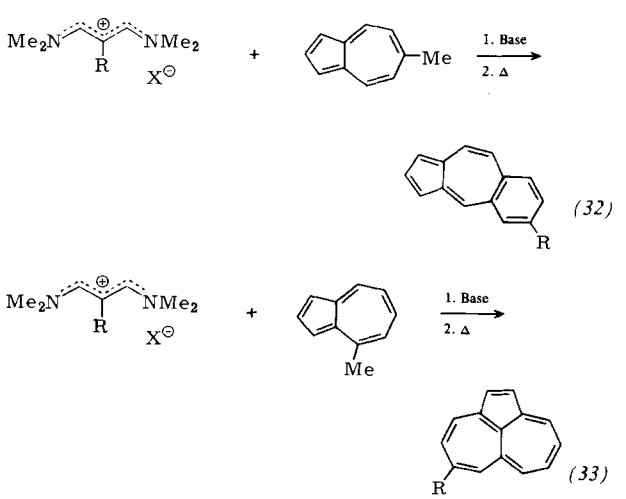


Z = F, Cl



(31)

Yet another interesting cyclopentadienide derivative, (31), was obtained by reaction of a vinamidinium salt with the reactive methyl group of the 1,4-dimethylpyridinium ion and subsequent displacement of the second amino group by cyclopentadienide ion[39].

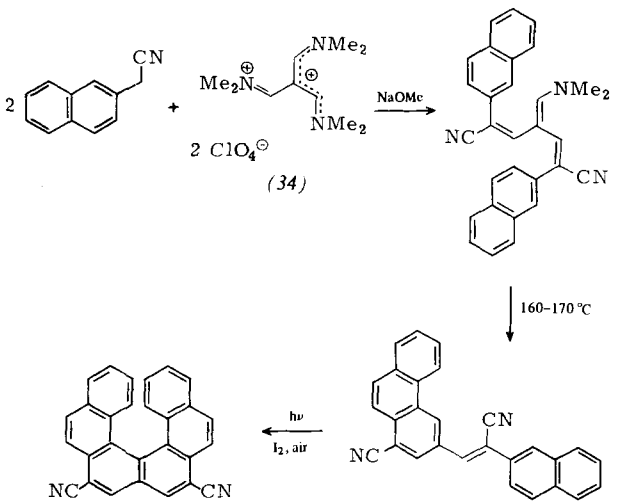


(32)

(33)

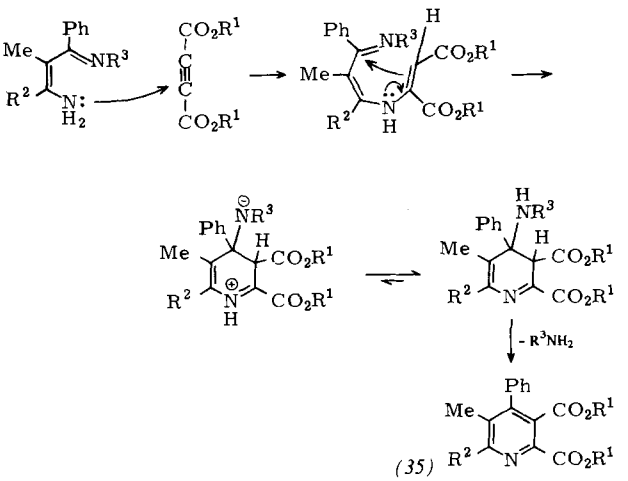
Methyl groups attached to the seven-membered ring of azulene can react as C—H acids; their reactions with vinamidinium salts have been utilized to prepare benzazulenes *(32)* and cyclopentaheptalenes *(33)*[36].

As a final example the interesting synthesis of hexahelicene using the iminiomethylvinamidinium salt *(34)* may be quoted[40].



(34)

A different type of reaction, which presumably involves the vinamidine behaving as a nitrogen nucleophile in addition



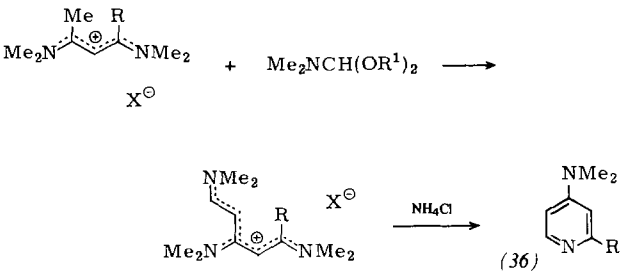
(35)

to undergoing nucleophilic attack, occurs with acetylenedicarboxylic esters, and results in the formation of pyridinedicarboxylic esters *(35)*[40a]. A possible mechanism is outlined below.

3.3. Reactions Involving α-Methyl Groups of Vinamidinium Salts

α-Methyl groups of vinamidinium salts have potential carbanionic reactivity, like that of α- and γ-methyl groups in pyridinium ions; but the synthetic possibilities that this provides have not yet been explored. One example which has been reported is the preparation of 4-(dimethylamino)pyridines *(36)*[41].

If R also represents a methyl group, reaction only takes place at one of the two methyl groups. As might be expected similar reactivity is not shown by β-methyl groups.

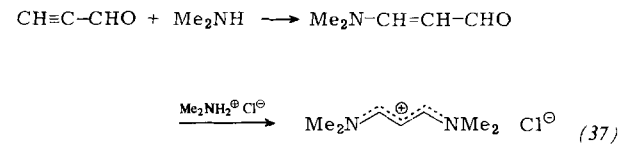


(36)

4. Preparation of Vinamidines and Vinamidinium Salts

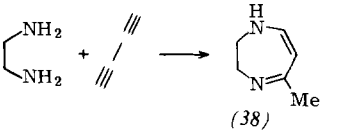
The two commonest methods for the preparation of vinamidines and their salts are the reactions of amines with α,β-alkynones or β-dicarbonyl compounds.

Thus one of the simplest and most commonly used vinamidinium salts is the 1,5-diazapentadienium derivative *(37)*, which has been prepared from propargaldehyde[42].



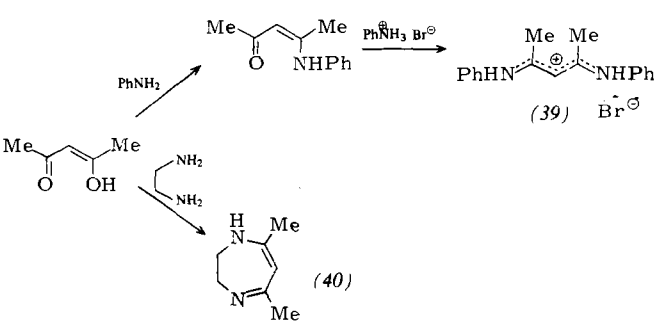
(37)

No cyclic analogs appear to have been made to date by reaction of alkynones with diamines, but the dihydrodiazepine *(38)* has been obtained by addition of ethylenediamine to a 1,3-diyne[43].



(38)

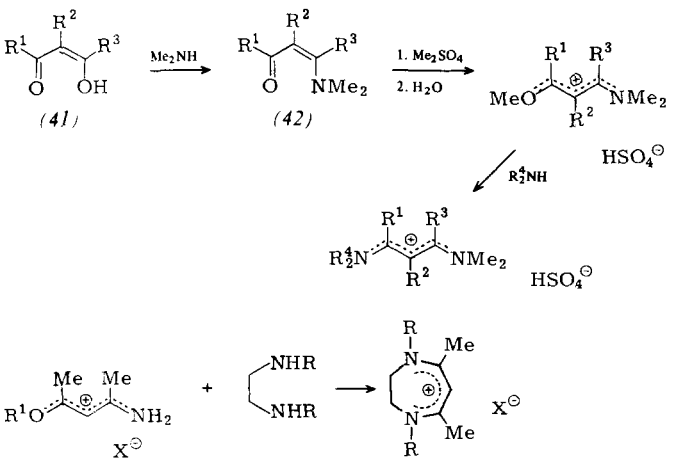
By contrast the reactions between β-diketones and amines have been used to prepare both acyclic[44] and cyclic[45] vinamidines, and their salts, *e.g. (39)* and *(40)*.



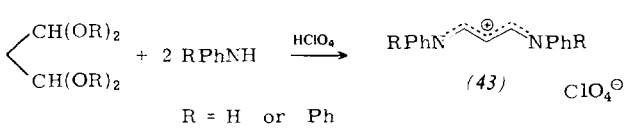
(39) *(40)*

A review of the preparation of dihydrodiazepines has already appeared in the literature[46].

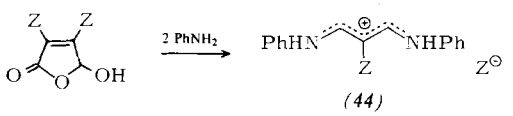
In the preparation of open-chain vinamidinium salts, *e.g. (39)*, the reaction is frequently carried out in two steps as shown in the above example[44]. An alternative stepwise process which is often advantageous involves alkylation of the intermediate oxoenamine *(42)*, followed by replacement of the alkoxy group by an amine[41,46a]. Diamines provide cyclic vinamidinium salts[47].



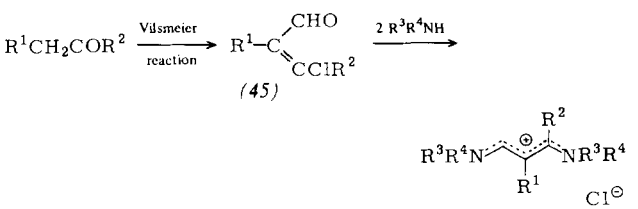
In place of dicarbonyl compounds *(41)* their monoacetals[11,48] or diacetals[8,49] may also be used. Thus the unsubstituted *N,N'*-arylvinamidinium salts *(43)* have been prepared from the tetracetal of malondialdehyde[8,23].



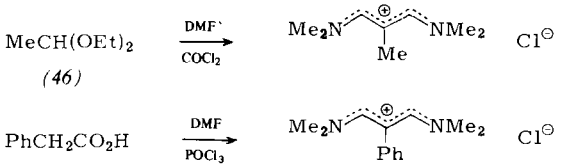
β-Halovinamidinium salts *(44)* have been prepared from mucochloric and mucobromic acids, which are masked β-dicarbonyl compounds[50].



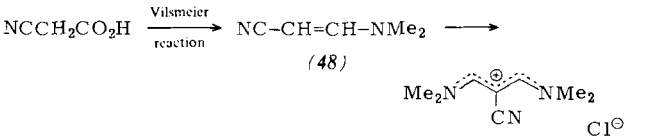
β-Chlorovinylaldehydes *(45)*, which may be regarded as the acid chlorides of the enol forms of β-dicarbonyl compounds, can also serve as starting materials for the preparation of vinamidinium salts[14,51,52]. Since the chloroacrylaldehydes are themselves readily prepared from α-methyleneketones[51,53] this serves as another convenient route to the salts. Vinamidines have also been obtained from β-chlorovinylketones[30a,53a].



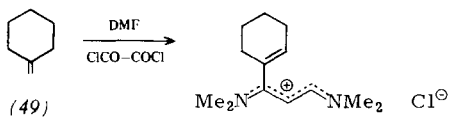
A third general method for the preparation of vinamidinium salts utilizes the Vilsmeier formylation of aldehyde acetals *(46)*[54], haloacetic acids[21,32,55,56], cyanoacetic acid[20], phenylacetic acids *(47)*[21,56] or malonic acids[57].



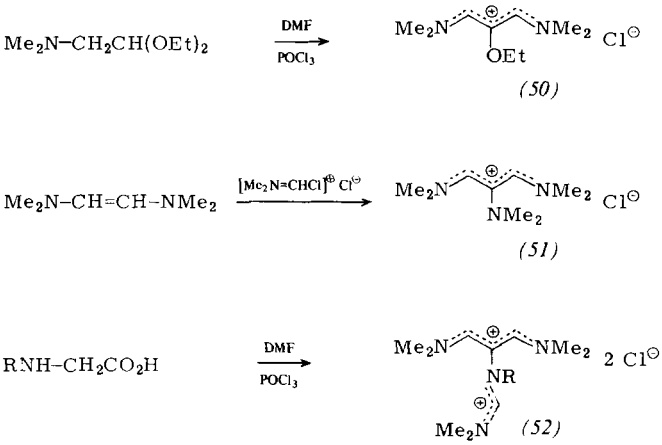
The mechanism of formation from the acids is not fully understood; however, it is known to involve diformylation coupled with decarboxylation. In the case of the reaction from cyanoacetic acid an intermediate *(48)* is obtained[20].



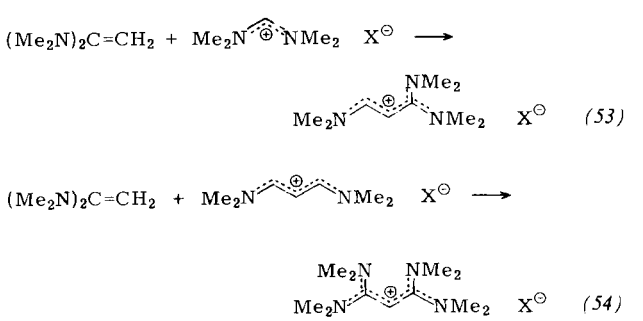
An example of the formation of a vinamidinium salt by Vilsmeier reaction of an alkene *(49)* has also been reported[58].



β-Alkoxy-[59] and β-aminovinamidinium salts[59], *(50)* and *(51)*, respectively, and *(52)*[60] have also been prepared by Vilsmeier-type reactions.



α-Amino- and α,α'-diaminovinamidinium salts *(53)* and *(54)* have been obtained by addition of an α,α-diaminoethylene to a formamidinium salt, and to an unsubstituted vinamidinium salt, respectively[61].

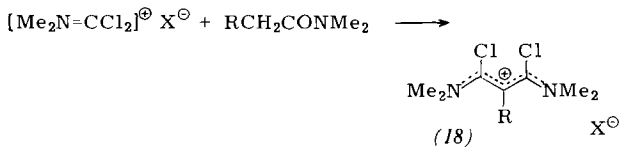


α-Aminovinamidinium salts of type *(53)* have also been prepared in high yield from the reaction between β,β-dichlorovinylketones and aniline[61a].

The synthetically valuable dichlorovinamidinium salts *(18)*, mentioned previously in Section 3.2 in connection with their use in the preparation of heterocycles, are obtained by reaction

of phosgene immonium salts with tertiary amines containing two α hydrogen atoms[28, 29, 62].

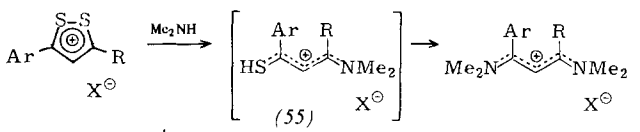
The dichloro compounds *(18)* have also been prepared by addition of phosgene immonium salts to alkynylamines[63].



(18)

Monochlorovinamidinium salts have been prepared by addition of phosgene immonium salts to enamines[28], and by means of a Vilsmeier reaction from *N,N*-dimethylamides containing two α hydrogen atoms[56]. Dibromovinamidinium salts are obtained by the action of hydrogen bromide on malononitrile[63a].

Two non-general methods which have provided vinamidine derivatives merit mention. α-Aryl and α,α'-diaryl derivatives are obtained when dithiolylium salts react with dimethylamine; the thiaaza salt *(55)* is postulated as intermediate[64].



R = H or Ar'

(55)

Dihydropyrimidines *(56)* are obtained by a "witches' brew reaction" from a ketone, a ketoacetal and ammonia in the presence of ammonium nitrate[65, 24].

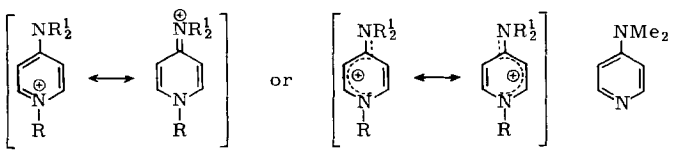
(56)

Finally the reader is referred back to Section 3.2 of this article which deals with reactions of vinamidines with nucleophiles. Examples are given of the interconversion of different vinamidines. Such interconversions are often most valuable for the preparation of specific vinamidines.

5. Special Vinamidines and Vinamidinium Salts

In natural product chemistry the corrins and porphyrins, which are of wide occurrence, contain vinamidine systems. Like their simpler analogs they undergo electrophilic substitution at the β-position[66].

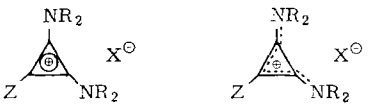
The 4-aminopyridinium system *(57)* is an example of a vinamidinium system which is electronically perturbed by a bridging alkene group.



(57) *(58)*

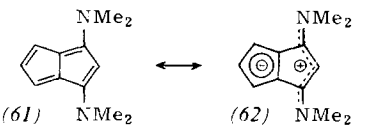
A detailed analysis of vibrational spectra of *(57)* (R = R' = H) shows that the vinamidinium structure is indeed the favored canonical form[67]. Nitration of the cation *(57)* (R = R' = Me) and of the free base *(58)* at the 3-position show similar rates over a wide pH range[68], which suggests that reaction proceeds *via* the cation and then by a typical vinamidinium mechanism (see Scheme 1).

Vinamidinium systems may play a part in stabilizing non-benzenoid systems. Two examples are the di- or triaminocyclopropenium salts *(59)*[69] and the diaminopentalene *(61)*[70].



Z = NR_2 or H

(59) *(60)*

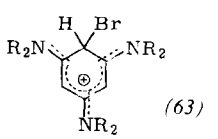


(61) *(62)*

Compound *(61)* unlike simple pentalenes, is stable in air for some hours. A helping factor here may be a contribution from the vinamidinium-cyclopentadienide canonical form *(62)*[70]. The aminocyclopropenium salts are stable in air and in particular are non-hygroscopic and very resistant to attack by water[69]. The bridged vinamidinium form *(60)* could contribute to stabilization in these compounds also. It would be extremely interesting to know if the diamino salts *(59)*↔*(60)*, Z = H, could undergo electrophilic substitution at the 2-position of the ring—unlike normal cyclopropenium salts but in keeping with vinamidinium character.

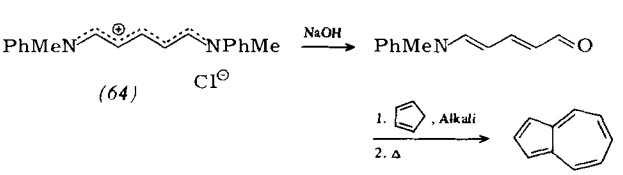
The ready protonation of the push-pull cyclobutadienes such as *(1)*, mentioned in Section 1, may also be assisted by the stabilization conferred upon the resultant ions by their bridged vinamidinium ion structure.

The vinamidinium system was also present in the first Wheland intermediates *(63)*, to be isolated and stable at ambient temperatures[70a].



(63)

Finally, mention should be made of the many vinylogs of vinamidines and vinamidinium salts. For example the readily accessible dianils of glutacondialdehyde *(64)*, prepared by the action of amines on pyridinium salts[42] are important synthetic intermediates, *inter alia*, in the synthesis of azulenes[71].



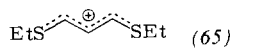
(64)

Like the vinamidinium salts their vinylogs also undergo electrophilic substitution, at the β-position[20]. Naturally occurring examples of such vinylogs are known[72].

Vinylogous vinamidinium salts are also of considerable commercial importance, for the cyanines, which are used as photographic sensitizers, all contain this structural feature. There is an enormous amount of literature available in this field; a review on cyanines comments that they "have made color photography and high-speed photography possible"[73].

6. Conclusion

There are many interesting aspects of the chemistry of vinamidines and vinamidinium salts. Some of the cyclic compounds of this type have been the subject of detailed study[46], but for the remainder, although there has been much information published about them, especially concerning their use in synthesis, there has been little in the way of systematic comparative studies. Thus comparisons of the effects of changing the amino groups have received little attention. Similarly the reactions of substituent groups, and the effects of such groups on the stability, structure and chemistry of the system, remain relatively little explored. It would also be



(65)

of interest to compare the properties of other hetero-analogs, *e.g.* compounds such as the dithiapentadienium ion *(65)*, whose spectrum has been reported[74].

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The Chemistry of Simple Phosphorus-Carbon Compounds

By Heinz Harnisch[*]

With the aid of selected examples an overview is given of the development trends in phosphorus-carbon chemistry over the past few years. An attempt is made to demonstrate the relationships between various parameters and properties such as constitution, basicity, substitution by functional groups, reaction behavior *etc.* of the compounds. In the case of basis compounds containing methylphosphorus groups the state of development of industrially interesting processes is also outlined. In addition, the synthesis of a few bifunctional phosphorus-carbon compounds which can be employed as comonomers in the production of polymers is described.

1. Introduction

The unique properties of the phosphorus atom offer the preparative chemist numerous reaction possibilities, the theoretical chemist the study of numerous phenomena, and the practically oriented researcher access to novel or extended applications in areas such as corrosion resistance, flame resistance, flotation, extraction, and complexation.

Phosphorus-carbon chemistry has gone through a phase of rapid development in the past few years. Research in this sector was stimulated in particular by the introduction of nuclear magnetic resonance spectroscopy, used for elucidating constitution, and the improved accessibility of starting compounds containing simple alkyl or arylphosphorus groups. In this review article an attempt will be made to outline some of the more important developments and findings of current interest in phosphorus-carbon chemistry.

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2. Properties and Reaction Behavior of Simple Phosphorus-Carbon Compounds

2.1. Influence of Basicity

The basicity of phosphorus-carbon compounds can be varied according to type and number of organic groups bound to the phosphorus. For example, in the series phosphane,

PH_3	CH_3PH_2	$(CH_3)_2PH$	$(CH_3)_3P$	$(CH_3)_3P{=}CH_2$ (*I*)
$[PH_4]^{\oplus}$	$[CH_3PH_3]^{\oplus}$	$[(CH_3)_2PH_2]^{\oplus}$	$[(CH_3)_3PH]^{\oplus}$	$[(CH_3)_4P]^{\oplus}$
4.31	4.04	3.95	3.88	3.82

Scheme 1. Basicity of the methylphosphanes. The figures below the cations are their relative electron densities (calculated after *Sanderson*).

methylphosphane, dimethylphosphane, trimethylphosphane the basicity of the respective compounds progressively increases, which phenomenon is also evidenced by the decrease in relative electron density of the corresponding phosphonium ions (Scheme 1).

Owing to the particularly large difference between the relative electron densities of PH_4^+ and $CH_3PH_3^+$ the three methylphosphanes can be easily separated from phosphane by treatment with moderately concentrated hydrochloric acid and formation of methylphosphonium ions. By increasing

the pH value the three methylphosphanes are again liberated, one after the other, sharply separated according to their basicity.

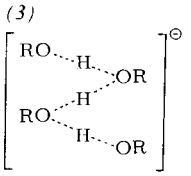
An even stronger base—trimethyl(methylene)phosphorane *(1)*—derives from the tetramethylphosphonium salts. Compound *(1)* can be prepared in good yield from tetramethylphosphonium chloride by splitting off HCl with sodamide according to a new method described by *Köster, Simić,* and *Grassberger*[1].

The ylide *(1)* is more strongly basic than ammonia and, as *Schmidbaur* and *Stühler*[2] have already shown, is therefore capable of converting many ammonium salts into the phosphonium salts, *e.g. (2)*.

$$(CH_3)_3P{=}CH_2 + NH_4SCN \longrightarrow [(CH_3)_4P]^{\oplus}SCN^{\ominus} + NH_3$$
(1) *(2)*

$$(CH_3)_3P{=}CH_2 + 4\ C_2H_5OH \longrightarrow (CH_3)_4POC_2H_5 \cdot 3\ C_2H_5OH$$
(1) *(3)*

$$(CH_3)_4POC_2H_5 \cdot 3\ C_2H_5OH \rightleftharpoons [(CH_3)_4P]^{\oplus}$$
(3)



(4)

Schmidbaur[3] has also proposed an ionic structure *(4)* for the alkoxyphosphoranes *(3)* obtainable by reaction of the ylide *(1)* with alcohols; the anions being bound *via* hydrogen bridges to molecules of the alcohol, which is present in excess. If the basicity of the alkoxyphosphorane is reduced by replacing the methyl groups by phenyl groups[4], progressively less stable products are obtained, the final representative, methylene(triphenyl)phosphorane *(7)*, forming only a labile adduct with methanol.

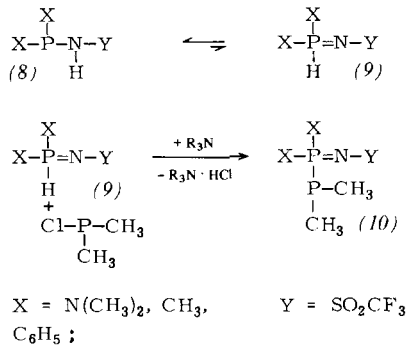
$$(CH_3)_3P{=}CH_2 + CH_3OH \longrightarrow (CH_3)_4POCH_3$$
(1)

$$(CH_3)_2C_6H_5P{=}CH_2 + CH_3OH \rightleftharpoons (CH_3)_3C_6H_5POCH_3$$
(5)

$$CH_3(C_6H_5)_2P{=}CH_2 + CH_3OH \rightleftharpoons (CH_3)_2(C_6H_5)_2POCH_3$$
(6)

$$(C_6H_5)_3P{=}CH_2 + CH_3OH \rightleftharpoons (C_6H_5)_3P{=}CH_2 \cdot CH_3OH$$
(7)

Schmidpeter and *Rossknecht*[5] made the interesting observation that a proton can be shifted from a neighboring amino group to the phosphorus by the presence of basicity-increasing methyl groups on the phosphorus. Imino(diorganyl)phosphoranes *(9)* usually transform spontaneously into the more stable aminophosphanes *(8)*. Tautomers with the P—H grouping could previously only be fixed in ring systems. However, the P—H structure can be forced in acyclic systems by dimethylamino or methyl groups on the phosphorus capable of increasing the basicity and by groups on the nitrogen that greatly increase the acidity. While P—H compounds containing dimethylamino ligands are stable, the corresponding methyl compounds can only be detected as labile intermediates. In the case of the phenyl derivatives the iminophosphorane—aminophosphorane equilibrium lies well over on the side of the amine *(8)*. A complete shift of the equilibrium can be achieved also in the case of the phenyl derivatives[6, 7] if the P—H tautomer is trapped in the form of compound *(10)* with chloro(dimethyl)phosphane.



(8) *(9)* *(9)* *(10)*

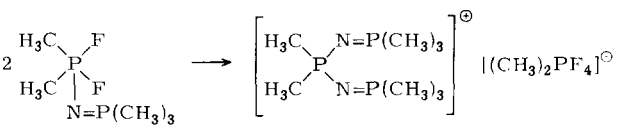
$X = N(CH_3)_2,\ CH_3,\ C_6H_5$; $Y = SO_2CF_3$ etc.

As shown in Scheme 1 the basicity of phosphorus compounds increases on progressive substitution with organic groups. This property was, *inter alia*, exploited for the synthesis of stable phosphonium ions. Conversely, the acidity, and thus stability of the corresponding anions can be reduced by substitution with organic groups. *Schmutzler, Hewson,* and *Peake*[8] have demonstrated this with the hexafluorophosphate ion. Tetrafluoro(organyl)phosphoranes *(11)* can be converted with

$$RPF_4 + CsF \longrightarrow Cs[RPF_5]$$
(11) *(12)*

$$RR'PF_3 + CsF \longrightarrow Cs[RR'PF_4]$$
(13) *(14)*

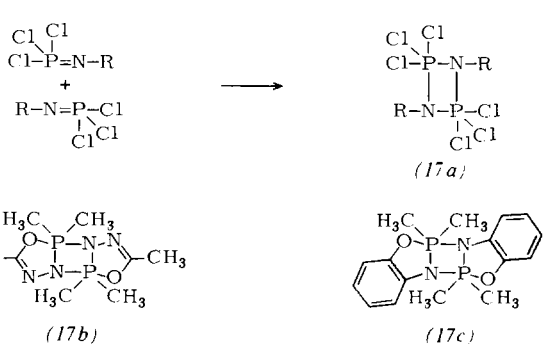
$R = CH_3,\ C_6H_5$; $R' = C_6H_5$



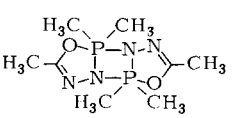
(15) *(16)*

CsF into cesium pentafluoro(organyl)phosphates *(12)*. Trifluoro(diphenyl)- and trifluoro(methyl)phenylphosphoranes are the only diorganylphosphoranes *(13)* with which this reaction has so far been accomplished; trifluoro(dimethyl)phosphorane cannot be transformed into the anion owing to too great a reduction of the acidity by the two methyl groups.

The preparation of compounds *(16)* containing the tetrafluorodimethylphosphate ion was finally achieved by *Schmutzler, Stelzer, and Stadelmann*[9, 10] by disproportionation of the iminophosphorane *(15)*. The dimethylbis(trimethylphosphoranediylamino)phosphonium ion exerts a strong donor action and thus stabilizes the labile anion.



(17a)



(17b)

(17c)

A similar situation arises in the case of the cyclic dimers of phosphazenes, the so-called diazadiphosphetidines *(17)*. Here also the only derivatives that are stable are those such as *(17a)* bearing strongly electronegative substituents on the pentacoordinated phosphorus, but not those with acidity-weakening methyl groups. Synthesis of the methyl compounds *(17b)* and *(17c)* is possible by energetically stabilizing the dimer by incorporation of five-membered rings[11-13]. [Cf. also compound *(63)* in Section 2.5.]

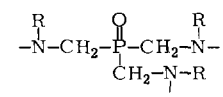
2.2. Influence of Functional Groups on the Phosphorus

Modification of the bonding on the phosphorus as a result of changing the basicity by organic substituents is also of considerable preparative importance. Another property of the P—C bond often plays a key role however: its high stability. This permits stepwise limitation of the reactivity at the phosphorus. The reactive inorganic "standard phosphorus compounds" such as PCl_3, PH_3, PCl_5, $POCl_3$, and even P_4 can undergo several reactions *via* the P—Cl, P—H, and P—P bonds and, where present, *via* the phosphorus lone pair; hence the course of the reaction is frequently of a complex nature. The selective use of only one or two reaction possibilities can therefore seldom be achieved. Consequently the isolation of mono- or bifunctional secondary products required for the synthesis of phosphorus-containing ring or chain molecules or for the fixation of stable side-groups, can be achieved only with difficulty and in poor yields from these compounds.

As a rule phosphane reacts with formaldehyde[14,15] up to the trifunctional tris(hydroxymethyl)phosphane *(18)* or in acidic medium up to the tetrakis(hydroxymethyl)phosphonium chloride *(19)*, which on further reaction, *e.g.* with amines or ammonia, form either highly cross-linked polymers *(20)* or even complex polycycles.

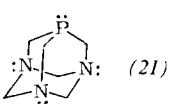
$$PH_3 + 3\ CH_2O \xrightarrow[Cd^{2+}]{} :P(CH_2OH)_3 \quad (18)$$

$$PH_3 + 4\ CH_2O + HCl \longrightarrow [P(CH_2OH)_4]^{\oplus}Cl^{\ominus} \quad (19)$$



(20)

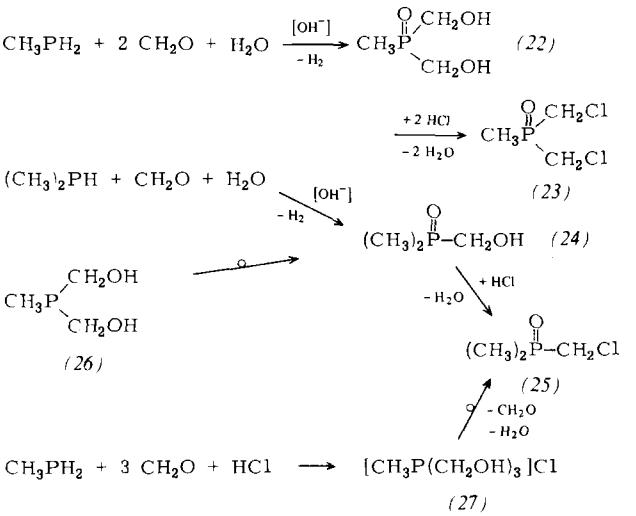
Thus *Daigle et al.*[16] as well as *Fluck* and *Förster*[17] have recently obtained 1,3,5-triaza-7-phosphaadamantane *(21)* from tris(hydroxymethyl)phosphane *(18)*, formaldehyde, and ammonium acetate.



(21)

If, on the other hand, one or two of the phosphorus valencies are "sealed off" with methyl groups the series of mono- and bifunctional P—C compounds becomes readily accessible.

In the presence of catalytic amounts of OH^- ions, the basis compounds CH_3PH_2 and $(CH_3)_2PH$ react with formaldehyde[18] and water as oxidizing agent with liberation of hydrogen and formation of bis(hydroxymethyl)methylphosphane



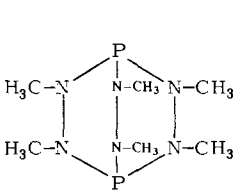
(22) *(23)* *(24)* *(25)* *(26)*

$$CH_3PH_2 + 3\ CH_2O + HCl \longrightarrow [CH_3P(CH_2OH)_3]Cl \quad (27)$$

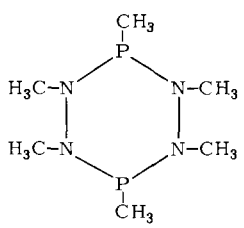
oxide *(22)* and hydroxymethyl(dimethyl)phosphane oxide *(24)*, which can be converted by reaction with hydrogen chloride into the chloromethyl compounds *(23)* and *(25)*, respectively[19]. The phosphane oxides *(24)* and *(25)* are also accessible *via* methylphosphane. Thus *(24)* can be obtained by rearrangement of *(26)*[20,21], and *(25)* by chlorination of *(24)* with HCl[19], as well as in one step *via* pyrolysis of the salt *(27)*[22,23] in which a rearrangement takes place.

The halogen compounds exhibit differences similar to those exhibited by the hydrogen compounds. Here also the reactions with PCl_3 are frequently more complex and yield end products having more complicated structures than in reactions with dichloro(methyl)phosphane or chloro(dimethyl)phosphane.

Thus, as *Nöth, Goetze*, and *Payne* have found[24,25], reaction of hydrazine or hydrazine derivatives with PCl_3 leads to bicyclic compounds of type *(28)* in moderate yields, whereas with dichloro(methyl)phosphane considerably better yields of the monocyclic compounds of type *(29)* are formed[26].

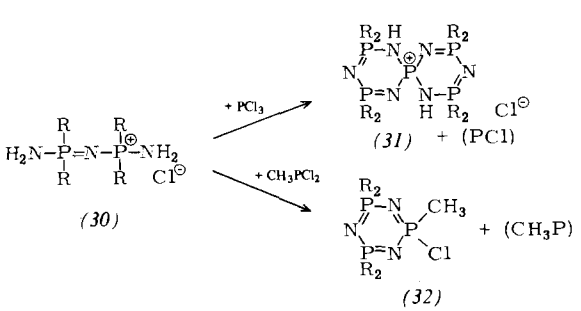


(28)



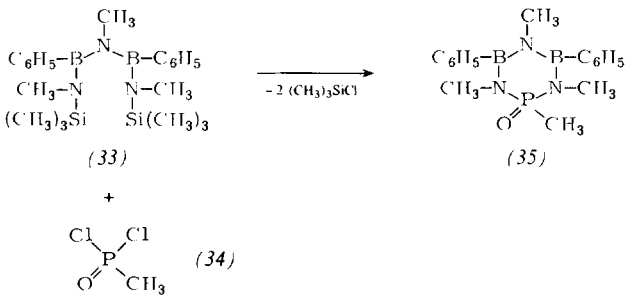
(29)

In the reaction of an aminodiphosphazene derivative *(30)* with PCl_5 investigated by *Schmidpeter* and *Eiletz*[27] a complex spirophosphonium salt *(31)* and an unidentified amorphous substance, designated here as (PCl), are formed. With dichloro(methyl)phosphane on the other hand, a monocyclic phosphazene *(32)* is obtained as end product.



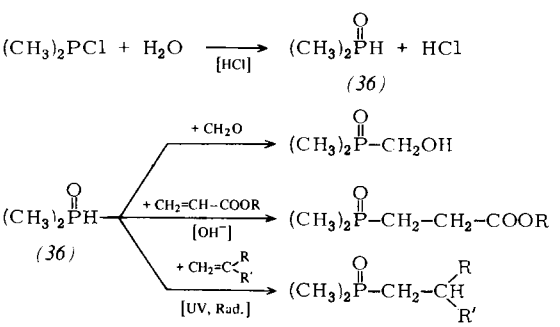
(30) *(31)* + (PCl) *(32)* + (CH_3P)

Like dichloro(methyl)phosphane, the easily accessible methanephosphonic dichloride *(34)* can also be employed for the synthesis of cyclic phosphorus compounds. Thus, *Nöth*[28] synthesized the triazaphosphadiboracyclohexane *(35)* by reaction of *(34)* and the terminally silylated aminoborane *(33)* with cleavage of the Si—N bonds.

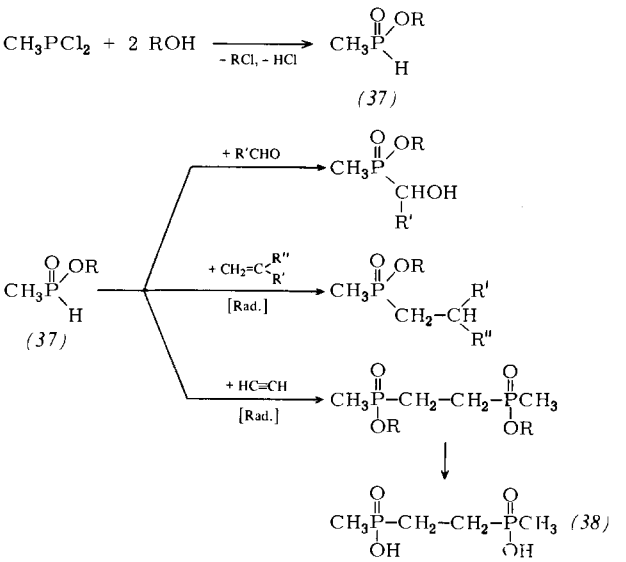


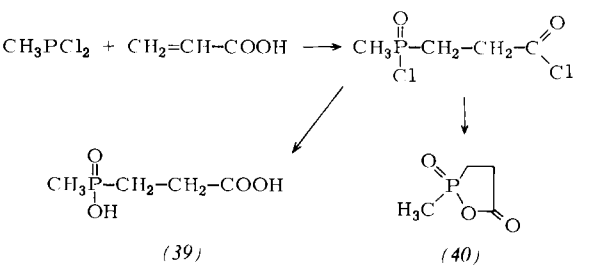
(33) + *(34)* → *(35)*

The chloro(methyl)phosphanes, just like the methylphosphanes, are also suitable for the preparation of numerous simple mono- and bifunctional secondary products. *Kleiner*[29] prepared the dimethylphosphane oxide *(36)* as a stable product in high yields for the first time by solvolysis of chloro(dimethyl)phosphane, a reaction affording entry to numerous possible reactions *via* the P—H bond, *e.g.* with olefins or carbonyl compounds.

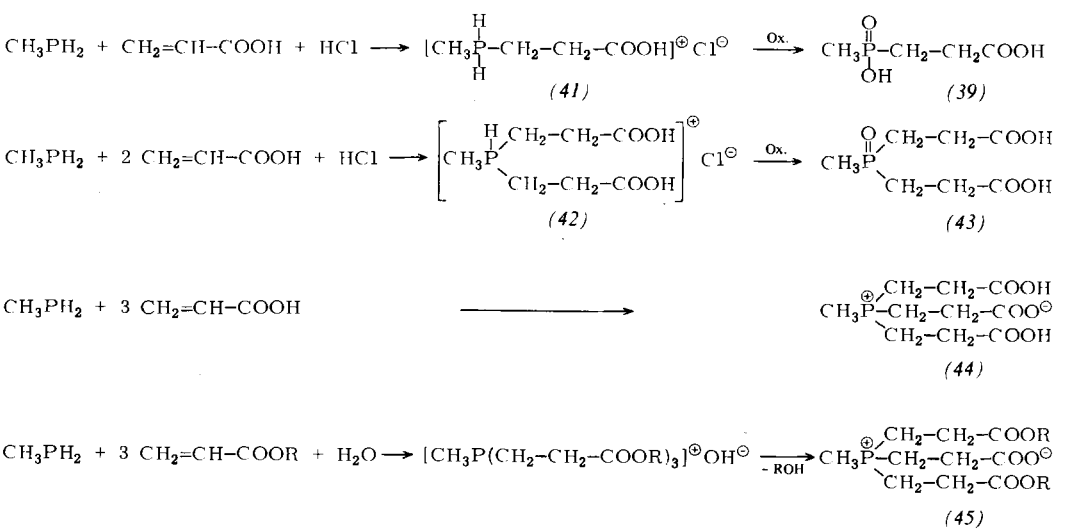


Reaction of dichloro(methyl)phosphane with alcohols furnishes methanephosphonates *(37)*, whose reactive P—H bond undergoes a large variety of reactions, *e.g.* with unactivated α-olefins or carbonyl compounds[30]. Reaction with acetylene gives ethylene-1,2-bis(methylphosphinic acid) *(38)*[31]. Dichloro(methyl)phosphane can also react directly with activated double bonds, *e.g.* with acrylic acid; this affords entry to the 3-[hydroxo(methyl)oxophosphorio]propionic acid ("2-carboxyethyl(methyl)phosphinic acid") *(39)* or its inner anhydride *(40)*[32].

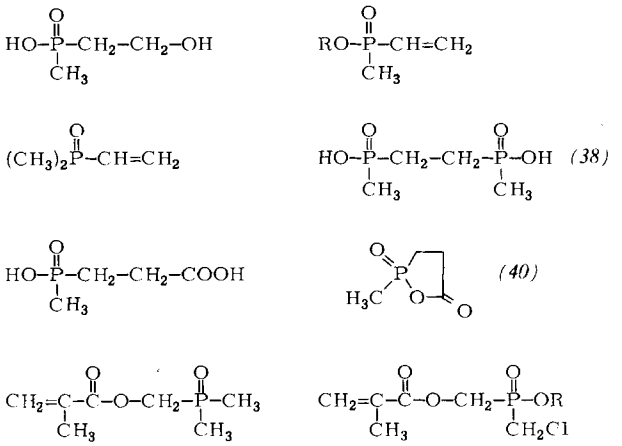




The acid *(39)* is also accessible from methylphosphane, acrylic acid, and hydrochloric acid[33]. Depending on the quantitative proportion of the reactants the initial product is either bis(2-carboxyethyl)methylphosphonium chloride *(42)* or 2-carboxyethyl(methyl)phosphonium chloride *(41)*, which on subsequent oxidation undergo smooth conversion into the



P-methyl3,3′-phosphonoyldipropionic acid ("bis-2-carboxyethyl(methyl)phosphane oxide") *(43)* and the acid *(39)*, respectively. Experiments to synthesise 3,3′-(methyl)phosphanediyldipropionic acid ("tris(2-carboxyethyl)phosphane") from methylphosphane and acrylic acid met without success. The biased inclination of phosphorus to coordination number 4 is so strong that the betaines are formed, which are stable both in the acid form *(44)* as well as in the ester form *(45)*[33].



Scheme 2. Phosphorus-containing comonomers.

At Hoechst AG a large number of compounds which can be employed as comonomers in the production of polyesters, polyacrylics, and polyamides have been synthesized using the parent substances CH_3PH_2, $(CH_3)_2PH$, CH_3PCl_2, and $(CH_3)_2PCl$ and the secondary products $(CH_3)_2P(O)H$ *(36)* and $CH_3P(O)H(OR)$ *(37)* as starting materials. Scheme 2 shows a few of these phosphorus compounds, which even in relatively small amounts have shown excellent flame resistant properties in the polymers produced, often without noticeable impairment of the mechanical or other properties of the polymers; this, *e.g.*, obviates the need for halogen compounds previously necessary in the case of polyesters.

2.3. Influence of the Organic Group on the Reactivity

In the examples mentioned so far the methylphosphorus compounds were favored as starting materials. Naturally many reactions can also be carried out with compounds having other alkyl or aryl groups on phosphorus. The methyl compounds, however, have been favored for the following reasons:

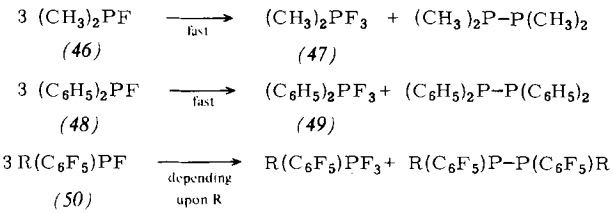
1) In contrast to *aryl*phosphorus chemistry, *alkyl*phosphorus chemistry has been the subject of research and investigation on a wide scale only since about 1960 and is in rapid development;

2) bulky alkyl or aryl groups readily mask the properties or desired effects of the phosphorus atom;

3) of the alkylphosphorus compounds the methyl compounds are the most readily available;

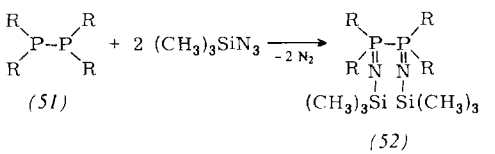
4) the methyl compounds are the most reactive phosphorus compounds without functional groups in the organic substituents. In this connection, both steric and electronic effects might play an important role.

Let us consider a few examples: *Fild* and *Stankiewicz*[34] have studied the disproportionation of the fluorophosphanes. Fluoro(dimethyl)- *(46)* and fluoro(diphenyl)phosphane *(48)* rapidly disproportionate to the phosphoranes *(47)* or *(49)* and the diphosphanes, respectively. If, however, one of the two organic groups is replaced by the pentafluorophenyl group, as in *(50)*, the rate of disproportionation is reduced to such an extent that marked differences in the sense of the quoted sequence of reactivities become noticeable.



$R = CH_3 > C_2H_5 > C_6H_5 > C_6F_5 > t\text{-}C_4H_9$

Appel and *Milker*[35] have investigated the reaction of tetraorganyldiphosphanes *(51)* with trimethylsilyl azide to give the silylated diphosphanediimides *(52)* and established a similar sterically determined dependence of the reactivity of the ligands on the phosphorus. Tetraphenyldiphosphane does not undergo reaction.

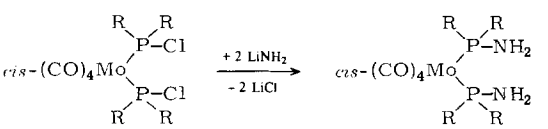


$R = CH_3 > C_2H_5 \approx C_3H_7 \approx C_4H_9 \gg C_6H_5$

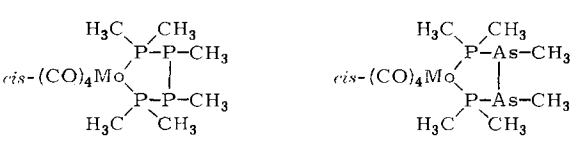
Stelzer, *Johannsen*, and *Unger*[36] were able to show in their investigations on reactions at the coordinated R_2PCl ligands of *cis*-disubstituted molybdenum complexes such as *(53)* that for steric reasons methylphosphorus compounds react with lithium amide to give the amines *(54)* more rapidly and in better yields than the phenyl derivatives (see also Section 2.4).

2.4. Metal Complexes with Organylphosphorus Ligands

Complexation to give *(54)*, $R = CH_3$, leads to stabilization of the amino(dimethyl)phosphane, which is unstable in the free state. *Stelzer* and *Unger* have synthesized the permethylated linear tetraphosphane *(55)* and the diphosphinodiarsane *(56)* from *(54)*, Li instead of NH_2, and CH_3PCl_2

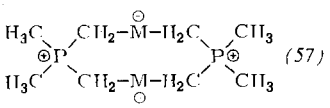


$R = CH_3 > C_6H_5$



and CH_3AsCl_2, respectively[37]. It is possible to stabilize labile compounds by use of the protective function of organic groups and their integration into transition metal complexes.

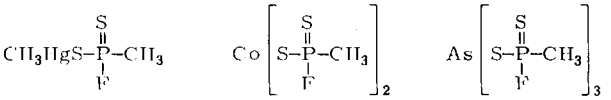
The synthesis of such metal complexes with organylphosphorus ligands has led to a considerable increase in the number of this class of substances being isolated in recent years. For example, *Schmidbaur*[38] has prepared complexes having rather unique structures by reaction of trimethyl(methylene)phosphorane *(1)* with metal salts; examples are the copper and silver complexes of type *(57)*.



(57)

M = Cu, Ag

Novel metal complexes of alkanedithiophosphonic fluorides *(58)*—*(60)* have been prepared by *Roesky et al.*[39].

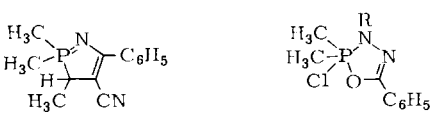


(58) *(59)* *(60)*

2.5. Cyclic Phosphorus-Carbon Compounds

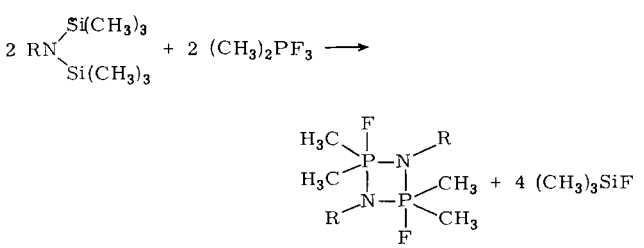
Also worth noting is the synthesis of numerous novel cyclic compounds containing organylphosphorus groups in the ring system. Some of these [*e.g. (29)*, *(31)*, *(32)*, *(35)*, and *(40)*] have already been mentioned in Section 2.2 in connection with the discussion of reaction principles.

Further examples are the 2,2-dimethyl-3*H*-1,2λ^5-azaphospholes *(61)* and oxadiazaphospholines *(62)* synthesized by *Schmidpeter*[13,49].



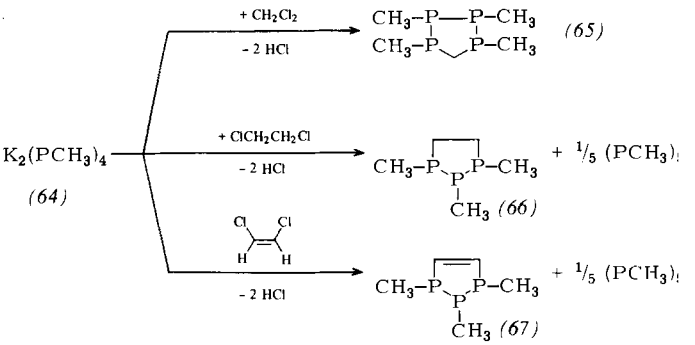
(61) *(62)*

Schmutzler[50] has employed fluoro(methyl)phosphoranes for preparation of the diazadiphosphetidines *(63)*, which at low temperatures exhibit *trans-gauche* isomerization at the phosphorus atoms.



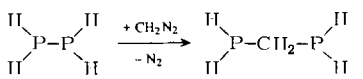
(63)

Heterocycles with cumulated phosphorus atoms can be prepared *via* the dipotassium compounds of organylcyclophosphanes. *Baudler et al.*[40-42] have synthesized tetraphosphacyclopentanes *(65)*, triphosphacyclopentanes *(66)* and triphosphacyclopentenes *(67)*, respectively, by reaction of the methyl- *(64)* and ethylphosphorus compounds with dichloromethane, 1,2-dichloroethane and *cis*-dichloroethylene in accordance with the reaction principle already practiced in the case of the phenyl compounds. Reactions with the C_2 dihalogen compounds do not lead, as one might expect, to six-membered rings, but rather to the obviously more stable five-membered rings.



(64) *(65)* *(66)* *(67)*

Recently the same team[43] investigated the reaction of diphosphane with diazomethane. It proved possible, for instance, to carry out simultaneous coupling of two P—C bonds and insertion of a methyl group between the two phosphorus atoms.



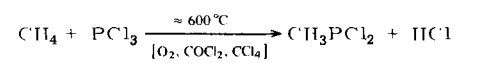
(68)

3. Industrial Synthetic Routes to Simple Phosphorus-Carbon Compounds

A challenging and diversified phosphorus-carbon chemistry can only acquire industrial utility if an economical synthesis of the P—C bond can be realized. Industrial phosphorus-carbon chemistry has so far been based almost exclusively on the di- and trialkylphosphites, compounds providing access to only a limited sector of this branch of chemistry. The paramount question then is: whether and how the versatile basis products CH_3PCl_2, $(CH_3)_2PCl$, CH_3PH_2, and $(CH_3)_2PH$ can be prepared on an industrial scale.

3.1. Chloro(methyl)phosphanes

CH_3PCl_2 was already produced for a limited period in the USA in the second half of the 1960's. The process developed by *Pianfetti*[44] uses PCl_3 and CH_4 as starting materials, which in the presence of homogeneous catalysts, such as O_2, $COCl_2$ or CCl_4, react at 550—600°C *via* a free radical mechanism with formation of hydrogen chloride:



With a brief residence time in the reaction zone and subsequent rapid chilling, yields of up to 85% can be achieved with a 15—20% conversion. Chloro(dimethyl)phosphane is not accessible in this way, since it is no longer stable at the temperature required for the desired reaction to take place.

Hoechst AG is presently operating a pilot scale plant based on this principle and having a capacity of a few tons of CH_3PCl_2 per month. The basic process has been developed by *Gehrmann* and co-workers (Hoechst AG). The product is to be used for the synthesis of halogen-free comonomers required for the production of flame-resistant polyester fibers. In this process, however, separation of the CH_3PCl_2 from excess PCl_3 is relatively difficult since their boiling points lie only about 7°C apart from each other, thus necessitating an involved rectification step.

The pilot-scale production of CH_3PCl_2 *via* a Kinnear-Perren complex *(69)* has been investigated by *Schliebs*[45]. PCl_3, CH_3Cl and $AlCl_3$ are used as starting materials. For the production of small amounts of material this process can have advantages over the Pianfetti process.

$$PCl_3 + CH_3Cl + 2\ AlCl_3 \longrightarrow [CH_3PCl_3]^{\oplus}[Al_2Cl_7]^{\ominus}$$

(69)

$$[CH_3PCl_3]^{\oplus}[Al_2Cl_7]^{\ominus} \xrightarrow[-\ NaAlCl_4]{+\ Al\ +\ NaCl} CH_3PCl_2$$

(69)

Ständeke[51] has investigated the simultaneous pilot-scale production of CH_3PCl_2 and $(CH_3)_2PCl$ by reaction of phosphorus vapor with methyl chloride on activated carbon catalysts at about 400°C.

$$P_4 + 6\ CH_3Cl \xrightarrow[[C_{akt}]]{\approx 400\,^{\circ}C} 2\ CH_3PCl_2 + 2\ (CH_3)_2PCl$$

The process is based on the work of *Maier*[46] and *Bretschneider*[47]. Reaction of phosphorus vapor with methyl chloride proceeds, like that of PCl_3 with methane, *via* a free-radical mechanism. By suitable modification of the process, particularly the addition of hydrogen chloride to inhibit decomposition of the chloro(dimethyl)phosphane that is formed, it was possible to increase the yield of the two major products to more than 80% referred to phosphorus. The overall conversion amounted to *ca.* 20%. The molar ratio of the major products can be altered relatively substantially. The main by-products that are formed are dimethylphosphane, trimethylphosphane and PCl_3.

A large-scale experimental plant based on this process has been operated for a period of time. Despite all efforts, however, the effective life of the catalyst could not be extended to an economically acceptable order of magnitude. At the temperatures required in the process decomposition of the methyl chloride leads to irreversible separation of carbon on the surface of the catalyst and to a large drop in activity.

3.2. Methylphosphanes

Hestermann[48] (Hoechst AG) has investigated the reaction of methyl chloride with PH_3 on activated carbon catalysts. The reaction proceeds at a satisfactory rate at 300°C. Methylphosphane and dimethylphosphane are the major products. A relatively large variation in the molar ratio of the two products is also possible in this process. The main by-products are phosphorus, arising from the decomposition of small amounts of pH_3, and tetramethylphosphonium chloride *(70)* which is formed *via* the trimethylphosphane on further reaction of $(CH_3)_2PH$.

$$PH_3 \xrightarrow[-\ HCl]{+\ CH_3Cl} CH_3PH_2$$

$$PH_3 \xrightarrow[-\ 2\ HCl]{+\ 2\ CH_3Cl} (CH_3)_2PH$$

$$(CH_3)_2PH \xrightarrow[-\ HCl]{+\ CH_3Cl} (CH_3)_3P \xrightarrow{+\ CH_3Cl} [(CH_3)_4P]^{\oplus}Cl^{\ominus}$$

(70)

$$4\ PH_3 \longrightarrow P_4 + 6\ H_2$$

The yield of the two major products has been reported to amount to 75%, based on phosphorus used. Methyl chloride does not decompose at the temperature of the reaction and the catalyst can be regenerated by removal of sublimed *(70)*. The space-time yield in this process is about three times higher than in the phosphorus process.

4. Conclusions

Intensive studies in the field of phosphorus-carbon chemistry by numerous research groups has led to many interesting and far-reaching developments in this sector. Such a multiplicity of theoretical and practical aims and approaches underly the investigations carried out in recent years that phosphorus-carbon chemistry, together with related branches of chemistry in which the properties of the phosphorus atom plays an important role, has become one of the most important as well as most interesting fields of molecular chemistry. It is to be hoped that this rapid development will also lead to a variety of new practical applications of phosphorus-carbon compounds.

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Solid State Chemistry of Ionic Fluorides

By Josik Portier[*]

The results of intensive pure research into the chemistry and physics of fluorides can be pieced together to give an overall picture whose discernible outlines hold promise of numerous new compounds having unusual and in some cases unique properties. Modern technology is called upon to exploit them.

1. Introduction

The properties of some fluorinated inorganic materials have been known since antiquity. However, systematic research in this area began less than one hundred years ago, after *Moissan* had succeeded in isolating elemental fluorine. Until 1940, research in the field of fluorine chemistry was limited due to technical difficulties. During the course of World War II, fluorine chemistry began to develop rapidly: the isotopic separation of uranium utilizing uranium hexafluoride required large quantites of fluorine. The handling of the gas was rapidly simplified because of the appearance of corrosion resistant materials, and by the industrial production of liquified hydrogen fluoride and compressed fluorine.

This spectacular development rapidly led to numerous applications, especially of fluorochlorohydrocarbons (freons), tetrafluoroethylene polymers (teflon), sulfur hexafluoride (for its dielectric properties), *etc.* The applications of solid inorganic fluorides are much more limited. One can mention AlF_3 in aluminum metallurgy and the use of various inorganic fluorides in organic fluorination.

A survey shows, however, that in the specialized journals of solid state physical chemistry, ten per cent of the publications are dedicated to fluorides. This interest of researchers for fluorine compounds far exceeds its present industrial application, suggesting that the potential applications of inorganic fluorides are numerous and varied. It is this aspect that we shall develop in this contribution.

2. The Fundamental Properties of the F^- Ion—Consequences for the Physicochemical Properties of Fluorides

Inorganic fluorides have specific properties which distinguish them from other compounds. Since these properties are due to the characteristics of the fluoride ion, it would therefore be logical to start by considering this ion and comparing its properties with those of its neighbors in the Periodic Classification, O^{2-}, S^{2-}, Cl^-[1].

Fluorine possesses the electron configuration $1s^2 2s^2 2p^5$. In the F_2 molecule each fluorine atom contributes an electron to a single covalent bond. The intramolecular distance is 1.435 Å. The dissociation energy of the molecule (37.8 kcal/mol at 298.15 K) is extremely low (O_2, 118.32; Cl_2, 58.02; S_2, 102 kcal/mol). Fluorine is the most electronegative element (F, 4.0; O 3.5; Cl, 3.0; S 2.5 on *Pauling*'s scale) and it will easily adopt the electronic structure of its noble gas neighbor neon ($1s^2 2s^2 2p^6$), leading to the F^- ion which is practically the only stable ionic form of fluorine.

These two properties, low dissociation energy of the molecule and very high electronegativity, explain the history of fluorine chemistry. Its late discovery by *Moissan* and the failure of earlier attempted preparations by *Davy, Ampère*,

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and *Faraday* are due to the fact that fluorine reacts with its environment immediately upon formation. It is now known that fluorine reacts with almost all the elements including noble gases—except helium, neon, and argon. Its handling is only possible because of the passivation of certain metals by a protective layer of a nonvolatile fluoride (nickel for example) or the chemical inertness of fluorinated polymers.

This extraordinary reactivity and the exothermic character of the reactions in which it is involved have interested researchers in the fields of rocket propulsion[2]. Indeed, on reaction with hydrogen it gives far higher combustion temperatures (4700 °C) than those obtained with oxygen (3250 °C). As a result, the specific impulse obtained is 380 s whereas it is less than 365 s with oxygen. The technical development of propellants which function with the F_2-H_2 couple has been hampered because of the high chemical reactivity of the halogen as well as the toxic nature of the combustion products. It seems, however, that some tests have been undertaken in the USSR and USA (NASA) with oxygen enriched with fluorine.

The extreme electronegativity of fluorine largely explains the properties of fluorides, which are due mainly to the localized character of the electron: covalence is weak and there are no known fluorides having metallic character.

The ionic radius of the fluoride is of the order 1.33 Å according to *Ahrens*. It is practically the smallest anion. Only the hydride ion in certain combinations has a smaller ionic radius ($\approx$1.20 Å). As a result, the F^- ion is highly mobile in crystal lattices. This property will be discussed later on.

Strong electronegativity and short cation-anion distances confer a high lattice energy upon the fluorides. Their melting and boiling points are therefore higher than those of the other halides. However, these temperatures are still nearly always lower for the fluorides than for the oxides, because the single negative charge of the F^- ion limits their coulombic energy.

3. Chemical and Crystallographic Properties of Fluorides

As a general rule, inorganic fluorides are very inert towards other elements; no halogen or chalcogen is able to displace F from its compounds. Instead, fluorination of oxides is always strongly exothermic:

$$Li_2O + F_2 \rightarrow 2LiF + 1/2\,O_2; \quad \Delta G^\circ_{500} = -144 \text{ kcal}$$
$$MgO + F_2 \rightarrow MgF_2 + 1/2\,O_2; \quad \Delta G^\circ_{500} = -177 \text{ kcal}$$
$$Fe_2O_3 + 3F_2 \rightarrow 2FeF_3 + 3/2\,O_2; \quad \Delta G^\circ_{500} = -278 \text{ kcal}$$
$$ZrO_2 + 2F_2 \rightarrow ZrF_4 + O_2; \quad \Delta G^\circ_{500} = -177 \text{ kcal}$$

A different situation arises when one comes to the hydrogenated compounds. Water and ammonia generally react with the fluorides giving rise in a first step to hydrogen fluoride having a very high bond energy (135 kcal/mol). For example, in the case of rare earth fluorides, the following reactions are observed[3, 4]:

$$LaF_3 + H_2O \rightarrow LaOF + 2HF$$
$$2LaF_3 + 4NH_3 \rightarrow La_2NF_3 + 3NH_4F$$

The final products are the oxides or nitrides.

The hydrolysis reaction constitutes a restraint to the practical application of fluoride. In fact, living in an environment in which the active principles are water and oxygen, the engineer tends to utilize the oxides whose preparation and handling are simpler than those of the fluorides.

F^- has an ionic radius close to that of O^{2-}. As a result, it is possible to replace oxygen by fluorine in a large number of oxides (Table 1). Owing to the differences in the ionic charges, this substitution leads to a change in the oxidation state of the cations. However, this substitution does not succeed in all cases. For instance, it does not seem possible to prepare solid solutions of sodium chloride type. Lithium fluoride does not react with magnesium oxide, although the respective radii of the anions and cations are very similar. In certain structures an ordered distribution of oxygen and fluorine occurs. This is the case, for example, in certain rare earth oxide fluorides. They have a cubic symmetry corresponding to anionic disorder at high temperatures, but display a trigonal symmetry at low temperatures corresponding to an order between oxygen and fluorine[3].

Table 1. Substitution of O^{2-} by F^- in oxide lattices.

Structure	Formula	Example	Mechanism
rutile	$AO_{2-x}F_x$	$VO_{2-x}F_x$	$O^{2-} + V^{4+} = F^- + V^{3+}$ [5]
spinel	$AB_2O_{4-x}F_x$	$Fe_3O_{4-x}F_x$	$O^{2-} + Fe^{3+} = F^- + Fe^{2+}$ [6]
garnet	$A_3B_3C_2O_{12-x}F_x$	$Gd_3Fe_5O_{12-x}F_x$	$O^{2-} + Fe^{3+} = F^- + Fe^{2+}$ [7]
fluorite	$AO_{1-x}F_{1+2x}$	$EuO_{1-x}F_{1+2x}$	$O^{2-} = 2F^-$ [3]

Like O^{2-}, OH^- has a similar ionic radius to F^-. There exist, for example, very extensive solid solutions between the fluorides and hydroxides of trivalent rare earths, corresponding to the formula $La(OH_{1-x}F_x)_3$[8].

The solubility of the oxide and hydroxide ions in the fluorides doubtless constitutes an important obstacle to research into fluorides. Such contamination, even in trace quantities, can drastically change the properties of fluorides and it should be carefully controlled.

In a given structure, the fluoride ion can co-exist with many other anions, *e.g.* those of other halogens (EuFCl)[9], chalcogens (LaSF)[10], and pnictides (ThNF)[11]. Although not a general rule, the tendency towards order between the two anions is here more pronounced than with oxygen. This is a consequence of the significant difference in ionic radii and also the difference in charge for the chalcogens and pnictides.

The similarity of the ionic radii of oxygen and fluorine (1.40 and 1.33 Å on *Ahrens'* scale) suggests a certain analogy

Table 2. Crystallochemical analogies between fluorides and oxides.

Formula	Coordination number of cation	Structure	Example
AX	6	NaCl	LiF and MgO
AX_2	6	rutile	MgF_2 and TiO_2
	8	fluorite	CaF_2 and ZrO_2
AX_3	6	ReO_3	VF_3 and ReO_3
ABX_3	12, 6	perovskite	$KMgF_3$ and $BaTiO_3$
AB_2X_4	4, 6	spinel	Li_2NiF_4 and $NiFe_2O_4$
AB_2X_6	6	trirutile	$LiFe_2F_6$ and Fe_2TeO_6
$A_3B_3C_2X_{12}$	4, 6, 8	garnet	$Na_3Li_3Fe_2F_{12}$ and $Y_3Fe_3Fe_2O_{12}$

between oxide and fluorine crystal chemistry. In fact, the same type of coordination and structure is found when the cations have close ionic radii (Table 2).

However, it seems that only a limited structural variety is open to fluorides. This is probably due to the more pronounced ionic character of the bond. Since the structure adopted depends almost solely on stereochemical factors, the influence of the crystal field or covalence being negligible, it can generally be predicted with relative ease. As an example one can cite the compounds of the 3d transition elements and of the monovalent elements with the general formula $A_xM_yF_z$ where all structures obey the following basic rules (Fig. 1):

- the transition element is always octahedrally coordinated by fluorine;
- the octahedra (MF_6) are either isolated or bonded *via* corners (this rule is true when the radius A of the cation lies between 1 and 1.5 Å);
- all the fluorine atoms participate in the formation of the octahedra[12, 13].

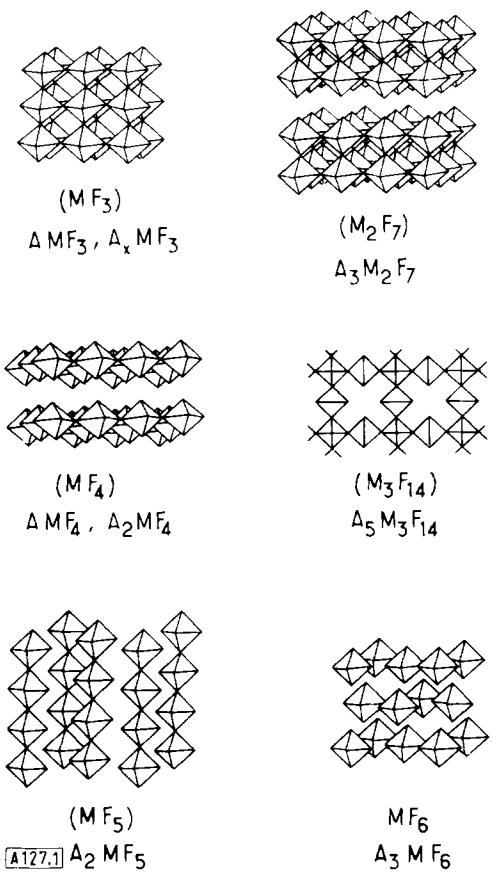

Fig. 1. Ideal arrangement of octahedra in transition metal fluorides $A_xM_yF_z$.

From the point of view of the crystal field theory, the ionic character of the fluorine-transition metal bond makes a weak field ligand of halogen. For the d elements this corresponds to a very weak splitting of the crystal field Δ_{CF}. This splitting is generally too weak to overcome the mutual repulsion of the d electrons, particularly for the first members of the 3d elements as well as for the end members with an oxidation state lower than three. These transition ions then adopt a high spin configuration (Fig. 2). With increasing covalence the crystal field splitting Δ_{CF} becomes greater, so that ligand field stabilization eventually permits electron pairing and low spin configurations may then be observed for the end members of the 3d series, and for 4d and 5d elements. The transition from one configuration to another is observed for nickel in oxidation state +3 (Table 3): the compounds of the A_3NiF_6 type (A = alkali metal) have a low spin configuration at low temperatures and high spin configuration above 100 K[14, 15]. However, in the oxides this transition already occurs for cobalt in the oxidation state +3. Since oxygen gives more covalent bonds than fluorine the crystal field splitting will be greater[16].

Table 3. Number and configuration (high spin ↑↑ or low spin ↑↓) of the d electrons of stable fluorides of the first transition series.

Element \ Oxidation state	+1	+2	+3	+4	+5	+6	+7	+8
Ti			1	0				
V		3	2	1	0			
Cr		↑↑ 4	↑↑ 3	2	1			
Mn		↑↑ 5	↑↑ 4	3				
Fe		↑↑ 6	↑↑ 5					
Co		↑↑ 7	↑↑ 6	5				
Ni		↑↑ 8	↑↓↑↑ 7	↑↓ 6				
Cu	10	↑↑ 9	↑↑ 8	7				

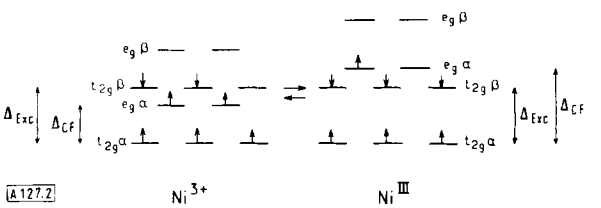

Fig. 2. High spin ⇆ low spin transition for Ni^{3+} compounds.

Fluorine is characteristically able to stabilize high oxidation states (Table 4). This particularly interesting aspect of fluorine chemistry has been studied by the German school under the guidance of *Klemm* and *Hoppe*[17]. This property arises from the pronounced electronegativity of fluorine. It is known that anions of lowest electronegativity stabilize the lowest oxidation states of cations, and the most electronegative anions, the highest oxidation states: iron reacts with iodine to give FeI_2, but with fluorine to give FeF_3. Since fluorine is the most electronegative element, one should expect to find the highest oxidation states in the fluorides. This hypothesis is sometimes true. For example, copper, silver, and gold do not appear to have an oxidation state higher than +3 in their oxides whereas copper and silver fluorides in the +4 oxidation state are known, and the +5 state has been reported for gold fluorides[18]. However, the opposite is often found to apply, as for iron, manganese, ruthenium, rhenium, and osmium. It is difficult to explain this paradox: two contradictory factors may be thought of as governing this phenomenon:

- the exceptional reactivity and electronegativity of fluorine favor the formation of high oxidation states;
- the ionic character of the metal-fluorine bond imposes a localization of the electrons around the fluorine and therefore a high formal cation charge. For a given oxidation state, this charge is weaker in the oxides where greater electronic delocalization appears owing to the formation either of covalent bonds or bonds having a metallic character. This delocalization diminishes the intercationic repulsions which become large for high oxidation states and therefore tends to increase the lattice energy.

Table 4. Maximum oxidation state of transition metals in oxides and fluorides.

Element	Maximum oxidation state		Examples
3d	O	F	
Ti	+4	+4	TiO_2; TiF_4
V	+5	+5	V_2O_5; VF_5
Cr	+6	+6	CrO_3; CrF_6
Mn	+7	+4	$[MnO_4]^-$; $[MnF_6]^{2-}$
Fe	+6	+3	$[FeO_4]^{2-}$; $[FeF_6]^{3-}$
Co	+4	+4	$[CoO_4]^{4-}$; $[CoO_6]^{8-}$; $[CoF_6]^{2-}$
Ni	+4	+4	$[NiO_6]^{8-}$; $[NiF_6]^{2-}$
Cu	+3	+4	$[CuO_6]^{9-}$; $[CuF_6]^{2-}$
4d			
Nb	+5	+5	Nb_2O_5; NbF_5
Mo	+6	+6	MoO_3; MoF_6
Tc	+7		Tc_2O_7
Ru	+8	+6	RuO_4; RuF_6
Rh	+4	+6	RhO_2; RhF_6
Pd	+4	+4	$[PdO_6]^{8-}$; PdF_4
Ag	+3	+4	$[AgO_6]^{9-}$; $[AgF_6]^{2-}$
5d			
Ta	+5	+5	Ta_2O_5; TaF_5
W	+6	+6	WO_3; WF_6
Re	+7	+6	Re_2O_7; ReF_6
Os	+8	+6	OsO_4; OsF_6
Ir	+4	+6	IrO_2; IrF_6
Pt	+4	+6	PtO_2; PtF_6
Au	+3	+5	$[AuO_4]^{5-}$; $[AuF_6]^{2-}$

It is interesting to compare the behavior of the fluorides and oxides as to nonstoichiometry. From the point of view of crystal chemistry, this behavior is not fundamentally different. There exist nonstoichiometric fluorides analogous to the oxides; to the oxides of uranium with the fluorite structure UO_{2+x} there correspond the fluorides of europium with the same structure, EuF_{2+x}[19]; the tungsten bronzes, M_xWO_3 have their homologous fluorinated isotypes M_xFeF_3[20]. However, it is conceivable that this tendency is less marked in the case of fluorides. Almost all the transition element oxides can contain insufficient or excess oxygen; variations in composition of the 3d transition oxides are often particularly large ($TiO_{0.69}$ to $TiO_{1.33}$). However, the corresponding binary fluorides generally have a constant composition. For example, in the iron-oxygen system under equilibrium conditions, two solid solutions are observed whose range extends from $Fe_{0.96}O$ to $Fe_{0.84}O$ and from Fe_3O_4 to Fe_2O_3 while in the iron-fluorine system only definite compositions are observed, FeF_2 and FeF_3 (Fig. 3). This fact should not be surprising; it is well known that the tendency to give definite compounds is all the greater when the electronegativity difference between the ions in the crystal is very high[21].

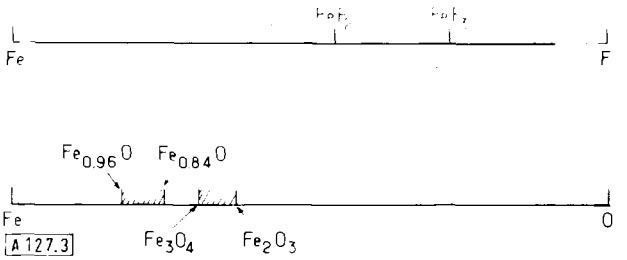

Fig. 3. Comparison between the iron-oxygen and iron-fluorine systems.

Another analogy between the oxides and fluorides is the tendency to form glasses: beryllium fluoride, like silica, combines with alkali fluorides giving glasses whose softening point is very low. The fluorinated glasses do not generally fuse with silicate glasses. This incompatibility, moreover, has been utilized in glassware production: the addition of sodium fluorosilicate to silicate glass brings about opaqueness which is due to the dispersion of the fluorides.

As previously pointed out, the ionic fluorides have moderate melting points associated with a pronounced chemical stability. In the molten state they are almost completely dissociated and have very good solvent properties. These properties suggest a number of applications. In fact, iron age metallurgists added fluorite to iron oxides to lower the melting point of the slag. Moreover, the word "fluor" signifies flow in Latin. It is this property which is used in aluminum metallurgy where bauxite is dissolved in a mixture of fluorite (CaF_2), cryolite (Na_3AlF_6), and aluminum fluoride.

This solvent property is also exploited in crystal synthesis. The crystal growth of many oxides can be accomplished from molten fluorides. One can cite the growth of YIG ($Y_3Fe_5O_{12}$) from melts of PbO and PbF_2.

Another application which appears very promising is the utilization of fluorides in molten salt nuclear reactors[22]. This last application offers a number of advantages over the classical solid fuel reactors, particularly in the area of safety. In addition, use of molten fluorides allows continuous elimination of neutron-absorbing fission products. The salts used in these reactors should possess the following properties:

chemical: stability at high temperature and under irradiation, strong dissolving ability for compounds of the fissile elements (U, Pu, Th);
physical: a moderate melting point, low vapor pressure, high thermal conductivity and thermal capacity;
nucleonic: weak neutron absorption and weak moderating action.

Fluorides satisfy all these requirements. Beryllium fluoride is used for its fusibility and lithium fluoride for its fluidity. The fluorides ThF_4 and UF_4 dissolve in this mixture.

Another related application of molten fluorides is their utilization for thermal energy storage[23]. Energy consumption is discontinuous while production is continuous. Various methods can be used to meet peak demands: electrochemical (batteries, hydrogen production by electrolysis of water); hydraulic (pumping of water into high reservoirs); mechanical (rapid rotation of flywheels). One elegant solution using fluorides has been proposed. Some eutectic mixtures of alkali or alkaline earth fluorides which have high heat capacities and heats of fusion are heated during the off-hours and subse-

quently liberate the absorbed heat on demand. This storage capacity per unit volume and weight is theoretically greater than for the conventional systems. In addition, the materials employed are cheap and abundant.

4. Physical Properties of Fluorides

In this report, we shall limit our attention to the more characteristic physical properties of saltlike fluorides, and to those having presently implementable or potential practical applications.

4.1. Electrical Properties

On the basis of the electronegativity of fluorine, the fluoride can be predicted to be insulators. They have, in fact, no appreciable electric conductivity. The gap between energy bands is usually large ($MgF_2 \Delta E \approx 12$ eV). Thus fluorides could be used for making capacitors, were it not for the fact that they are poor dielectrics: their permittivity is not very high in general, but when it is, they show high dielectric losses (Table 5)[24]. This last property can be explained by an anionic conductivity. As the smallest anion except for the hydride ion, the fluoride ion is highly mobile and one observes that fluorides have a higher anionic conductivity than oxides. Thus PbF_2 which has a similar structure to ZrO_2 is a much better conductor than its oxygenated homolog (Fig. 4). This result can, moreover, be generalized. An ionic solid has an ionic conductivity approaching that of the liquid near its melting point. As a consequence, the lower the melting point, the higher the conductivity. PbF_2 melts at 855 °C, ZrO_2 at 2700 °C.

These properties of fluorides have already been utilized in ion specific electrodes allowing the determination of fluoride ions in solution. They contain a LaF_3 crystal whose conductivity has been raised by doping with EuF_2. On one side of the crystal is placed a normal solution of F^- ions, and on the other side the solution to be measured. The apparatus works as a concentration cell: a potential difference is established between the two solutions which is proportional to the logarithm of the ratio of their concentrations. A calomel or a silver chloride electrode (Fig. 5) serves as standard.

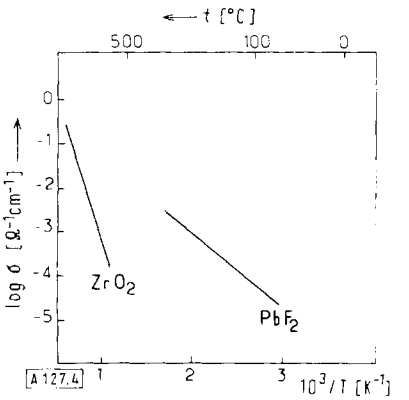

Fig. 4. Change of ionic conductivity with temperature in ZrO_2 and PbF_2.

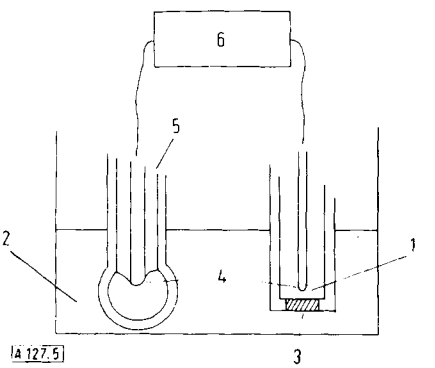

Fig. 5. Ion-specific electrode for fluoride determination (Orion Laboratories). 1, standard solution; 2, sample solution; 3, $LaF_3(EuF_2)$ crystal; 4, Ag/AgCl; 5, reference electrode (Orion recommends an Ag/AgCl electrode with electrolyte bridge and ground glass diaphragm); 6, potentiometer.

Table 5. Relative dielectric constant (ε_r') and loss factor ($\tan\delta$) of some fluorides.

Structure	Coordination number	Fluoride	ε_r'			$\tan\delta \times 10^4$		
			−50 °C	+25 °C	+150 °C	−50 °C	+25 °C	+150 °C
NaCl [a]	6	LiF	6	6	8	7	10	300
		TlF	9	9	440	100	600	100000
Rutile [a]	6	MgF_2	10	10	10	20	20	130
		MnF_2	15	15	20	30	40	2600
		ZnF_2	25	30	2000	100	500	10000
CaF_2	8	CaF_2	10	10	20	10	100	30000
		SrF_2	12	12	14	20	50	1000
		BaF_2	10	10	10	20	20	100
		CdF_2	30	35	1000	100	1000	10000
		PbF_2-β	40	45	7000	100	800	60000
Distorted ReO_3 type	6	AlF_3	6	6	6	80	100	200
		ScF_3	7	7	9	90	100	500
		InF_3	9	9	25	90	200	4000
YF_3	9	YF_3	6	6	7	30	80	600
		GdF_3	7	7	11	20	80	3000
		BiF_3	50	50	3000	100	800	60000
Tysonite	11	LaF_3	60	60	1000	200	1000	120000
ZrF_4	8	ZrF_4	10	10	10	20	40	200
		ThF_4	15	15	15	50	200	30000

[a] Or related structure.

The development of electrochemical generators with a solid electrolyte similar to those used in the galvanic chain S/β-Al_2O_3/Na can be envisioned. The negative electrode would be composed of a light and reducing metal such as lithium and the positive electrode composed of an easily reducible fluorinated material, such as the fluorides of some transition elements noted in Section 3 (Fig. 6). The change in free energy of such a system is very high and the voltage produced in such a cell should therefore be very high. By applying *Nernst*'s law to the apparatus depicted and by neglecting the reaction of the positive electrode, one obtains a theoretical voltage of more than six volts. However, the practical application of such an apparatus is limited by the relatively weak ionic conducticity of the known materials, which limit the current flow.

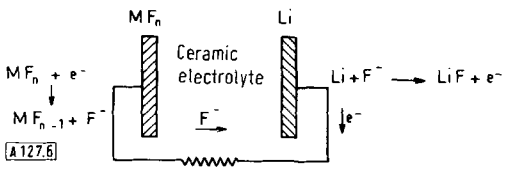

Fig. 6. Electrode reactions in a fluorinated solid electrolyte primary battery.

Other similar devices have been tested; the solid electrolyte was replaced for example, by an aprotic electrolyte ($LiClO_4$ in solution of propylene carbonate), the positive electrode is a carbon fluoride C_xF, and the negative electrode is lithium. The voltage in the open circuit is 3.5 V; the energy densities 3000 Wh/kg[25].

As an alternative to the solid electrolyte generators and those using a liquid electrolyte, a cell has been proposed which contains a low-melting eutectic mixture of fluorides as electrolyte. The positive electrode is the fluoride of a metal having a high oxidation state and the negative electrode is magnesium. The set-up is heated almost to the melting point of the eutectic. The generator discharges in a few minutes due to the great mobility of F^- ions in the molten salts. It was intended to use this apparatus, capable of furnishing a high energy during very short periods, for firing upper stages of space rockets.

Another electrochemical apparatus exploiting the anion conductivity of fluorides deserves mention. A thin layer of LaF_3 is placed between a grid-shaped gold cathode and a reactive anode of bismuth (Fig. 7). The characteristics of the cell depend on the atmosphere in which it is placed. When this atmosphere contains reducible gases (O_2, NO, SO_2) the current strength rapidly increases for a given applied potential V_c. The potential V_c is characteristic of the gaseous species in contact with the cathode while the current is proportional to the concentration of the gas. This device therefore behaves like a selective electrode. This phenomenon is interpreted as a reduction of gas at the cathode, followed by transport of the reduced species in the electrolyte and an oxidation step at the anode. The same cell can function as a fuel cell. Exposed to oxygen it gives in open circuit a voltage of 1.5 V with a lanthanum anode[26].

As previously mentioned (Section 3), fluorine can replace oxygen in a large number of oxides. This substitution naturally involves some modifications of their electric properties. Generally, one observes an increase in resistivity. The observed phenomenon can, however, be more complex: when fluorine is substituted for oxygen in a transition metal oxide, $M^{2n+}O_n^{2-}$,

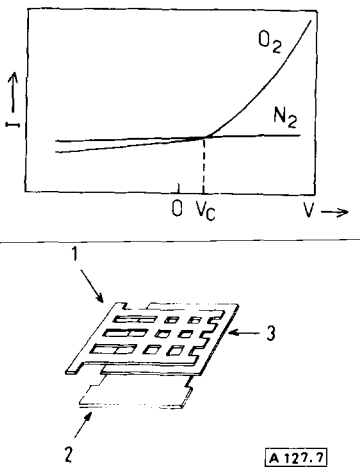

Fig. 7. Gas electrode using solid electrolyte (Philip Morris Research Center, after *Laroy et al.*). 1, grid cathode; 2, anode; 3, LaF_3 electrolyte.

a decrease in the cation charge is necessary to conserve electroneutrality $[M^{2n+}_{(1-x)}M^{(2x-1)+}_x O_{n-x}F_x]$. This corresponds to introduction of an extra d electron into the system. The properties will result from a competition between the localization of electrons by fluorine and increase in the number of these electrons. In VO_2, for example, which shows a semiconductor to metal transition there is first of all an observable decrease in the transition temperature which corresponds to a stabilization of the metallic phase and also a gradual progressive disappearance of the metallic character; VOF is again a semiconductor[5].

Studying the Mössbauer effect of compounds containing the same element in two different oxidation states clearly illustrates the localized character of the electrons in the fluoride in comparison with the chalcogenides or pnictides. The oxides or sulfides of this type are generally semiconducting with a low resistivity while the fluorides remain insulators. Figure 8 shows the Mössbauer spectra for $LiFe^{II}Fe^{III}F_6$[27] and for $Eu^{II}Eu^{III}_2S_4$[28]. For the first compound, the peaks corresponding to Fe^{2+} and Fe^{3+} appear, while for the second, above a certain temperature, only one peak shows up corresponding to a chemical shift intermediate between Eu^{2+} and Eu^{3+}. If in the fluoride the d electrons remain localized, in the sulfide a hopping phenomenon appears such that the Eu^{2+} and Eu^{3+} ions are no longer distinguishable.

The influence of the substitution of oxygen by fluorine on the properties of the ferroelectric oxides has also been studied. It involves a decrease in the Curie ferroelectric temperature which is easily explained by the ionic character of the metal-fluorine bond. The paraelectric-ferroelectric transition is tied to the alignment of the dipole moments, which involves the distortion of the crystal lattice, and is responsible for the spontaneous polarization (P_s) when $T < T_C$. This orientation of the dipoles is a function of the interatomic bonds in the material. It is the directional property of the covalent bond which is responsible for the alignment. The introduction of the strongly electronegative fluoride ions weakens the covalence of the bonds and therefore disturbs the alignment of

the dipoles; the value of P_S is then lowered and consequently so is T_C. The Curie temperature of $Sr_2KNb_5O_{15}$ is 420 K for example, whereas it is only 100 K for $SrK_2Nb_5O_{14}F$[29].

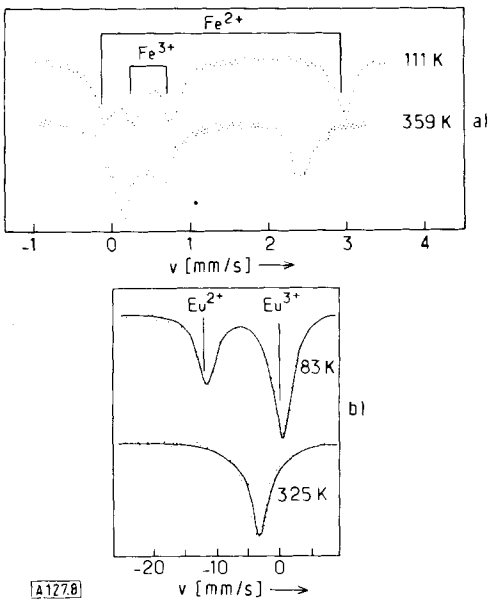

Fig. 8. Electron delocalization illustrated by the Mössbauer effect: a) spectra of $LiFe_2F_6$ [27]; b) spectra of Eu_3S_4 [28].

In the case of the ceramics this substitution also leads to an increase in dielectric constant and a decrease in dielectric losses. The use of these materials for the production of capacitators has been proposed[30].

4.2. Magnetic Properties

Numerous publications are concerned with the magnetic properties of fluorides. This interest of physicists for these materials has several reasons:

- Since fluorides are insulators, their magnetic properties are not influenced by electron delocalization such as often occurs in the oxides or sulfides. The interpretation of the phenomena is therefore simplified.
- Fluorides are transparent in a large spectral range, thus permitting magnetooptical studies.
- A large variety of structures is found in the crystal chemistry of fluorides, in which the transition element is octahedrally coordinated by fluorine. The arrangement of these octahedra makes possible the formation of three-dimensional (AMF_3), two-dimensional (A_2MF_4), and one-dimensional structures (A_2MF_5) each corresponding to a particular magnetic behavior (Fig. 1).
- Fluorine (^{19}F) has a nuclear spin $I=1/2$ and lends itself, therefore, to NMR experiments which permit determination of the percentage of covalence of the metal-fluorine bonds. In this respect it offers an advantage over oxygen whose commonest isotope ^{16}O has zero nuclear spin.

The magnetic behavior of transition element fluorides is not basically different from that of other insulating solids. Hence diamagnetic, paramagnetic, antiferromagnetic, and ferrimagnetic compounds are all represented.

4.2.1. Diamagnetic Compounds

Certain ions of the transition elements whose d layers are partially filled are diamagnetic. This requires an even number of more than 5d electrons and a low spin configuration (Table 3). In the 3d series, this only applies to tetravalent nickel. By contrast, in the 4d and 5d series, where the increase of the covalence involves a reinforcement of the crystal field, almost all such ions are diamagnetic (exception Pd^{2+}).

4.2.2. Paramagnetic Compounds

In the case of transition elements, paramagnetism will be found for those structures whose metal ions are isolated from one another; in other words, when the octahedra do not share any common atom. This is the case for compounds of composition AMF_6, A_2MF_6, A_3MF_6 (Fig. 1), for which the susceptibility generally follows Curie's law.

Trivalent nickel deviates in its behavior: the low-spin/high-spin transition leads to a change in moment of 1.73 μ_B to 3.7 μ_B[14].

In the case of rare earth metals paramagnetic behavior is generally observed.

4.2.3. Antiferromagnetic, Ferrimagnetic, and Ferromagnetic Compounds

When fluorides have structures such that the MF_6 octahedra are no longer isolated but share common geometric elements (corners, edges, faces), a magnetic order appears. Antiferromagnetic or ferrimagnetic properties are then observed. In fact, it is known that the energy which couples two spins S_i and S_j contains an exchange term:

$$H_{ij} = \sum_{ij} J_{ij} S_i S_j$$

The exchange integral J_{ij} is a function of the overlap of the d orbitals of the i-th and j-th atoms. For the transition metal fluorides this overlap is direct when the octahedra are linked either by faces or by edges (Fig. 9a). When the octahedra are linked by corners, a fluorine atom intervenes between the two paramagnetic atoms. The orbitals of i and j therefore overlap by superexchange involving the p orbitals of fluorine (Fig. 9b).

The type of interaction depends on the sign of the exchange integral J ($J<0$ antiferromagnetic, $J>0$ ferromagnetic interaction) and the intensity of the interaction, which is directly linked to the ordering temperature, is also dependent on J.

For an antiferromagnetic compound the Néel temperature is given by:

$$T_N = -\tfrac{2}{3}\frac{J}{k} ZS(S+1)$$

where k is *Boltzmann*'s constant and Z the number of nearest magnetic neighbors.

The exchange integral J is directly linked to the covalence of the bond. It can be shown that for a coupling using a σ bond of the type shown in Figure 9b, $J=-2b^2/U$. In this relationship U is the electrostatic repulsion energy brought about by the electron transfer from one ion to another. For the perovskite $KNiF_3$ for example, U is the energy which separates

the ground state $Ni^{2+}F^-Ni^{2+}$ from the excited state $Ni^{3+}F^-Ni^+$. The transfer integral b_σ depends on the overlap of the d and p orbitals. If E_d and E_p represent respectively the energies of the d and p orbitals concerned, b is equal to $f_\sigma(E_d - E_p)$; f_σ being the fraction of the d electron transferred from the d orbital to the p orbital. The transfer coefficient therefore depends on the covalence of the bond. For $KNiF_3$, f_σ is equal to 3.8 %.

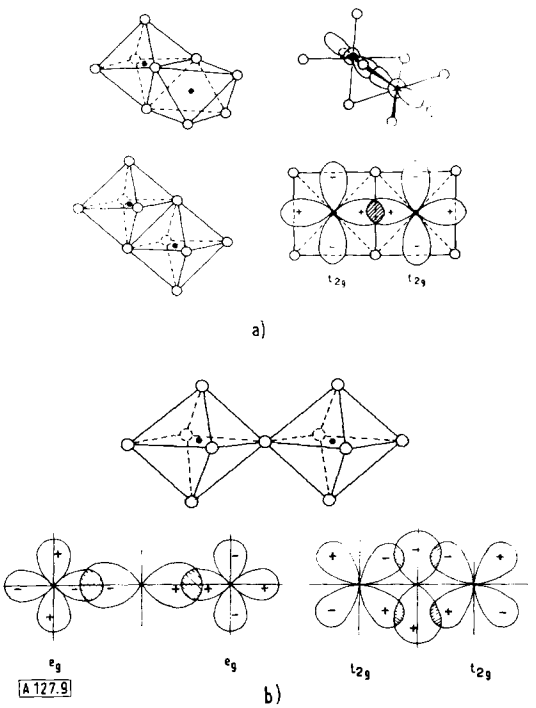

Fig. 9. Bonds involved in magnetic interactions (see text).

The sign of J can be predicted from the rules of *Goodenough-Kanamori*. If electron transfer occurs between one half-occupied orbital and another, the interaction is antiferromagnetic. This is the case for $KNiF_3$ which involves overlapping of the orbitals $d_{(x^2-y^2)}$-p-$d_{(x^2-y^2)}$ (Fig. 9b), the $d_{x^2-y^2}$ orbitals containing only one electron. By contrast, if this same transfer occurs from an occupied or half-occupied orbital to an unoccupied orbital, the interaction will be ferromagnetic as in the example of $Ni^{2+}Mn^{4+}(F^-)_6$ (Fig. 9b) in which a transfer is brought about from the half-occupied e_g orbital of Ni^{2+} to an empty e_g orbital of Mn^{4+}[31].

The preceding considerations allow a comparison between fluorides and oxides. If the same mechanisms are operative, the sign of the interactions will be identical: $LaFeO_3$ and $KMnF_3$ with a perovskite structure are both antiferromagnetic with the same magnetic structure, the Fe^{3+} and Mn^{2+} ions being isoelectronic (d^5). By contrast, the strength of the bonds in a given crystallographic structure will differ: the oxides have a much higher ordering temperature than the fluorides. Although $LaFeO_3$ and FeF_3 both have similar antiferromagnetic structures, the oxide has a Néel temperature of 738 K while that of the fluoride is only 394 K. The exchange integral for a fluoride is therefore only half the size of that in the corresponding oxide.

As a general rule, the ordering temperatures of fluorides are lower than room temperature and practical applications in the field of magnetism are hardly to be expected. Two fluorides, however, are the exceptions to this rule: FeF_3 and CoF_3. They are antiferromagnetic but have a weak ferromagnetism below their Néel temperatures, which are respectively 394 and 460 K. Owing to its transparency in the visible range, a practical application of the magnetooptical properties of FeF_3 was envisioned. In fact, this fluoride could be used as memory material in the treatment of information in the same manner as the lanthanoid orthoferrites. The information is inscribed in these materials by orienting the moments in a small domain of the crystal called a "bubble", which can be displaced by applying a magnetic field. The "bubble" can be usually observed by illuminating the crystal in polarized light because the plane of polarization of the light is rotated in an opposite sense when the light crosses opposing magnetization zones. The ray which crossed the bubble therefore does not have the same polarization as that which crossed the surrounding matter. Unfortunately, the use of FeF_3 is hampered by the difficulty in obtaining large crystals. At room temperature FeF_3 shows a trigonally distorted ReO_3 structure, and becomes cubic at 410 °C. The methods of growing large single crystals generally work above this temperature and therefore the crystallographic transition occurring at 410 °C during the cooling process produces strong internal tension which destroy the single crystal.

The ferrimagnetic fluorides constitute a particularly interesting class of materials (Table 6)[32]. It should be noted that their structures differ from those of ferrimagnetic oxides. In the oxides (spinels, garnets, hexagonal ferrites) the ferrimagnetism arises from the occupation of tetrahedral, octahedral, or dodecahedral sites by the transition elements. The magnetizations of the sublattices thus formed are in opposition (Fig. 10). In the fluorides only the octahedral sites are occupied by the transition element cations and both magnetic sublattices

Table 6. Characteristic data of ferrimagnetic transition metal fluorides [32].

Structure	Compound	T_C [K]	Θ_p [K]	σ_0 [μ_B]
Chiolite	$Na_5V_3F_{14}$	21	48	1.94
	$Na_5Cr_3F_{14}$	18	32	2.97
	$Na_5Fe_3F_{14}$	90	95	4.98
	$Na_5Co_3F_{14}$	108	110	3.10
Hex. $BaTiO_3$	$RbNiF_3$	145	300	0.76
	$TlNiF_3$	150		
	$CsFeF_3$	60	85	1.31
	NH_4NiF_3	150		0.1
	$CsNiF_3$	111		0.53
	$CsCoF_3$	50	65	0.8
$Cs_4Mg_3F_{10}$	$Cs_4Ni_3F_{10}$	15	106	0.06
	$Cs_4Co_3F_{10}$	33	120	0.98
Weberite	Na_2NiFeF_7	90	50	1.5
	Na_2NiCrF_7	4		
	Na_2NiCoF_7	126		0.9
	$Na_2Fe_2F_7$	84		0.75
	Na_2CoFeF_7	80		1.2
	Ag_2NiFeF_7	103		2.1
	Ag_2NiCrF_7	10		
$MnAlF_5$	$MnAl_{0.45}Fe_{0.55}F_5$	34	136	
Cr_2F_5	$CrTiF_5$	26	78	1.78
	$CrVF_5$	40	51	0.86
Hex. Cs_2NaCrF_6	Cs_2MnCoF_6	53	61	1.99
	Cs_2MnNiF_6	61	78	2.40

are therefore composed of octahedra. Ferrimagnetism results then from the way in which the octahedra are joined. In the fluorides of the $BaTiO_3$ type (hexagonal), for example, one of the sublattices consists of octahedra linked by corners and in the other sublattice the octahedra are linked by faces. For the chiolites the octahedra of one of the sublattices are linked by the two corners while in the second they are linked by four corners. In the ferrimagnetic fluorides of the type $MnAlF_5$ the octahedra are linked *via* edges for one of the sublattices and *via* corners for the other.

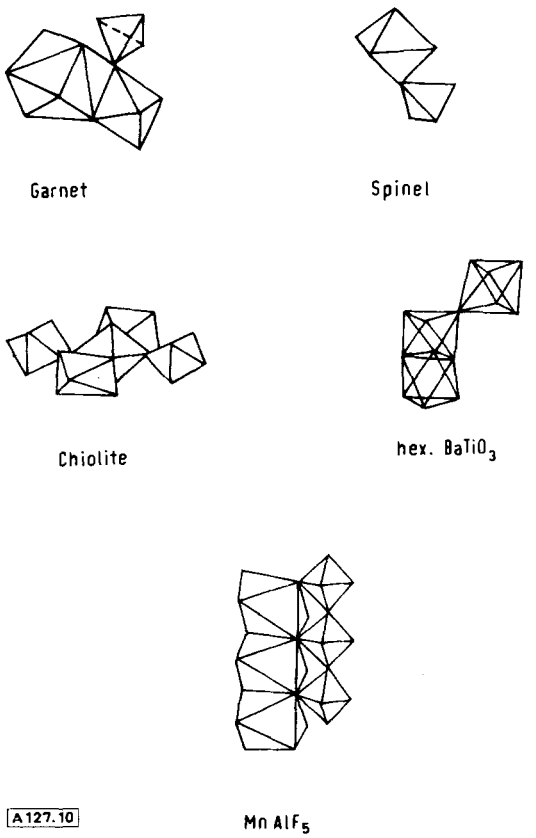

Fig. 10. Arrangement of polyhedra in ferrimagnetic oxides and fluorides.

Very few ferromagnetic fluorides are presently known (K_2CuF_4, TbF_3, $LiTbF_4$), but further examples will probably be discovered in due course.

4.3. Optical Properties

The optical properties of saltlike fluorides are typically those of insulators and therefore are not, in principle, different from those of other halide or oxide insulators. The interesting characteristics of the F^- ion give rise, however, to some unique properties which will be discussed below.

When an insulating crystal, free of defects, is exposed to a beam of photons of increasing energy, one first observes absorption bands corresponding to vibrational transitions. With increasing incident energy of the photons, the absorption bands corresponding to the electronic transition between cation orbitals appear (d-d, f-f, d-f, s-p, ...). The next absorptions to appear are charge transfer bands arising from electron transfer from the anion to the cation (Fig. 11). We will now examine these different regions of the optical spectrum.

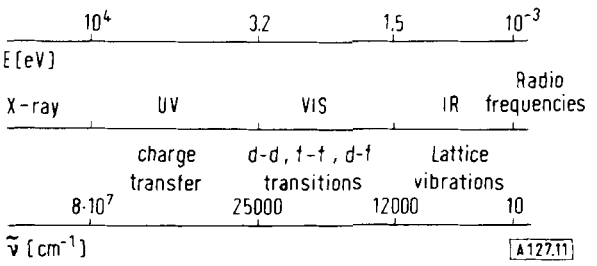

Fig. 11. Interaction between light and crystal as a function of photon energy.

As previously shown in Section 4.1, fluorides are insulators with a large band gap. As a result, the compounds of the elements not absorbing in the visible range (*i.e.* the lighter elements and those for which the d and f layers are full or empty) will be transparent up to the UV region. Magnesium fluoride, for example, as a perfect crystal, will be transparent from $10^6\,cm^{-1}$ (corresponding to the energy threshold where transitions from the valence to the conduction bands occur) to $10^3\,cm^{-1}$ (maximum frequency of lattice vibrations).

The transparency of fluorides has led to their use as windows or prisms in optical instruments. Another well known application is the use of thin layers of magnesium fluoride for coating lenses to decrease reflections and increase the luminosity. These thin layers of magnesium fluoride are also condensed onto solar panels for space satellites.

This property renders fluorides particularly attractive as host lattices for the luminescent ions. In fact, the luminous energy produced by these ions will sustain a very weak decrease by parasitic absorption in fluorinated materials.

At the other end of the spectral range of interest, *i.e.* the infrared, the fluorides do not behave differently from other compounds, in particular, the oxides. The excitation frequencies depend primarily on the mass of the vibrating atoms. They are generally located below $1000\,cm^{-1}$ for fluorides as well as oxides.

Let us now examine the electronic spectrum of the d and f transition elements which are located in the visible and ultraviolet range[33, 34].

For the d elements, for which the electronic levels responsible for those transitions correspond to the external orbitals which are subjected to the ligand field, two types of absorption are observed. The most intense absorptions come from charge transfers, transfer of the p electron of the ligand to the d orbitals of the central ion; they are allowed by *Laporte*'s rule. The weakest correspond to internal transitions in the d configuration and are therefore forbidden by this same rule.

In the fluorides, the transfer of an electron from the F^- ligand to the central atom requires a large amount of energy due to the electronegativity of the halogen. As a result, the corresponding absorptions appear in the ultraviolet range and are not visible. This explains the relative transparency of fluorides as compared with oxides or chlorides: the crystals of FeF_3 are slightly green in hue while those of $FeCl_3$ are deep violet and those of Fe_2O_3 are brown and almost completely opaque. This property renders the fluorides particularly attractive for magnetooptic research and applications.

The spectroscopic properties of compounds containing lanthanoids are of great practical value. The important applica-

tions to which these materials lead are well known, such as the laser operating with a YAG crystal ($Y_3Al_5O_{12}$) doped with neodymium or television screens using the fluorescence of the yttrium oxide sulfide doped with rare earths.

The spectroscopic properties of 4f elements are notably different from those of the d elements. The principal difference derives from the fact that the 4f electrons are protected from the crystalline field by external shells. The energy levels are therefore discreet and result in narrow spectral lines. Another difference is the ability of the lanthanoids to afford fluorescent spectra while this phenomenon is only rarely observed for the d elements. This behavior can be understood when one looks at the configuration curves in Figure 12. The curves of lower energy correspond to the ground level, and those of higher energy to the excited states. The distance r represents the distance from the cation to the anion which is not exactly the same for the two states. In the case of lanthanoids the minimum of the excited state is found inside the ground state curve. Since these minima in the configuration curves are almost superimposed, an excitation can be followed by an emission (Fig. 12a). In contrast, for the d elements which are less well protected from the crystal fields Δr varies considerably and the minimum of the configuration curve of the excited state is found outside of that of the ground state. The system then returns to the ground state without emission, with energy being dissipated by nonradiative emission (Fig. 12b)[35].

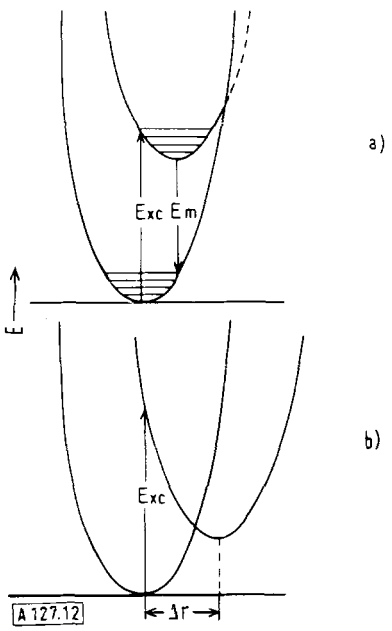

Fig. 12. Diagram of configuration curves for a) a luminescent center and b) a non-luminescent center.

Although the 4f orbitals mix only slightly with the anion orbitals, a certain covalence effect nevertheless exists. This leads to a broadening and to a red shift of the f levels. In the fluorides the covalence will clearly be the weakest, and their absorption and fluorescent spectra are therefore characterized by narrow bands identical with those of isolated ions.

A word should be said about the lifetime of the excited levels. Like the d-d transitions, the f-f transitions are theoretically forbidden by *Laporte*'s rule. They are observed, however, because the wave functions of the electrons taking place in these transitions do not have a pure f character but also a certain amount of p character due to covalency. It is in the fluorides that the f character will be most marked owing to the ionic nature of the bond. Several results derive from this. The more a transition is forbidden, the weaker will be the corresponding emission. In addition, the life of the excited state will be greater as the forbidden state becomes narrower, for a system will return all the more quickly to its ground state if the transition which accompanies this change is possible. It can be then concluded that fluorides have some weak spectral lines and that the duration of the excited states will be long.

The luminescence phenomenon in the rare earth compounds often results from energy transfer. The ion responsible for luminescence, which is named the activator, cannot receive energy directly but only through another ion called the sensitizer (Fig. 13). The sensitizer can be another cation [$(Ce, Tb)F_3$, $S=Ce^{3+}$, $A=Tb^{3+}$] or an anion [$(Y, Eu)VO_4$, $S=VO_4^{3-}$, $A=Eu^{3+}$][35]. The energy transfer requires a mixing of the

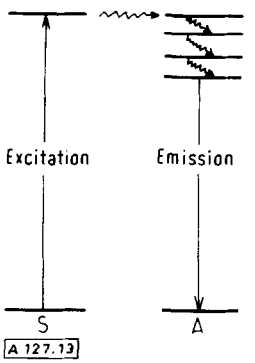

Fig. 13. Energy transfer from a sensitizer (S) to an activator (A).

wave functions of S and of A. In the fluorides, the activator cation is separated from the sensitizer ion by the F^-. The single charge of the fluoride ions leads to high coordination numbers (9 in YF_3, 11 in LaF_3) and the transfer phenomena are possible only by superexchange. Now as we have seen, the overlap of the f orbitals of lanthanoids and the p orbitals of fluorine are weak and the energy transfer difficult. As a result, the fluorides are generally less efficient luminophores than oxides.

This conclusion should, however, be qualified. In the case of the divalent lanthanoids, the energy difference which separates the $4f^n$ and $4f^{n-1}5d^1$ configurations are much smaller than in the case of trivalent rare earths. To the transitions which involve the 5d levels, there correspond large and intense absorption bands as in the case of the 3d elements. In addition, some nonradiative transitions can occur from this band to a 4f excited level which in turn allows an intense fluorescence (Fig. 14).

It is understood that in order to obtain high emission yields it is desirable to have as high a concentration of the activator as possible. However, if this concentration goes beyond a certain value the yield diminishes rapidly. If the probability of transfer from one activator cation to another becomes large as a result of the concentration, the energy of excitation is dissipated in the lattice in the form of heat and no longer contributes to luminescence. In the fluorides

these transfers are difficult due to the blocking effect of fluorine and the critical concentration will be much higher than for the oxides.

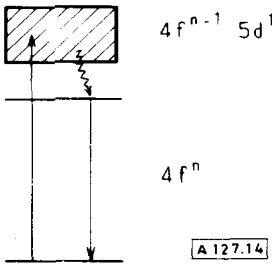

Fig. 14. Energy transfer within a divalent lanthanoid ion.

The transparency of the fluorides in the ultraviolet range, as was previously noted, will likewise play a double role. Excitation generally occurs in this wave length range. If the luminescence directly involves the activator, this property will be advantageous because no excitation energy will be dissipated in the lattice. In contrast, the F^- ions will be poor sensitizers compared with such ions as VO_4^{3-}, BO_3^{3-}, and PO_4^{3-} which readily effect transfers.

This set of specific properties helps in defining the areas of applications of rare earth fluorides. Generally, fluorides are not such good luminophores as oxides for the reasons mentioned above. On the other hand, however, their use has been proposed in the area of lasers for example, as binary or ternary fluorides of yttrium doped with neodymium. The reasons behind this choice are good transparency in the ultraviolet range, which leads to favorable behavior on excitation, slight attenuation, and a sharpness of the emission ray. Nevertheless, these devices do not appear to offer any great advantage over the oxides.

In the field of infrared to visible conversion, fluorides have proved to be exceptionally well suited, and are supplanting the other materials[36]. Efficient up-conversion is observed in the compounds containing two rare earth ions such as Yb^{3+} and Er^{3+} (Fig. 15). The levels of these ions are such that $A_2-A_1 \approx B_2-B_1 \approx B_3-B_2$. The following process takes place: the Yb^{3+} ion absorbs an energy photon $h\nu_1$ in the infrared range and is excited from the A_1 level to the A_2 level. Excitation transfer then occurs between neighboring Yb^{3+} and Er^{3+} ions; the Yb^{3+} ion falls back to the A_1 level and the Er^{3+} ion is promoted from the B_1 level to the B_2 level. If the excited state B_2 has a sufficient lifetime, which is the case with the fluorides, a second photon $h\nu_1$, can be absorbed by Yb^{3+} (transition $A_1 \rightarrow A_2$) before the Er^{3+} ion returns to the ground state. A second excitation transfer is then possible, the Er^{3+} ion moving into the B_3 state while

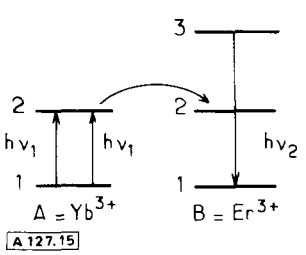

Fig. 15. Conversion of infrared into visible light.

the Yb^{3+} ion falls back to the A_1 level. The final return of the Er^{3+} ion from B_3 to B_1 leads to the emission of a photon $h\nu_2$ such that $\nu_2 \approx 2\nu_1$. The frequency $2\nu_1$ is located in the visible range.

This process can be generalized as the successive energy addition of three, or even four identical photons, or also as the energy addition of two photons of different energies. In this latter case, the fluorescence photon $h\nu_3$ obeys approximately the relationship $\nu_3 \approx \nu_2 + \nu_1$, where ν_1 and ν_2 are the frequencies of the two incident photons.

This phenomenon aroused considerable interest when it was shown that the yield is considerably improved by using Yb^{3+} as the sensitizer ion. It is often called the "Auzel effect" after its discoverer[36].

This mechanism effects the transformation of an infrared radiation into green light by addition of two photons, or into blue light by addition of three photons. Several applications have been envisioned. The Auzel effect can be utilized in quantum meters for detection and visualization of infrared radiation. Electroluminescent diodes are also feasible: a fluoride doped with ytterbium and erbium or with thulium is deposited in powder or single crystal form on the surface of a gallium arsenide diode emitting in the infrared. The radiation is transformed by the fluoride into visible blue or green light. Fluorinated matrices which lead to better yields are alkali-yttrium fluorides.

Yet another phenomenon capable of application has recently been discovered[37]. It involves not only the f-f transitions which were previously noted, but also f-d transitions. While the transfer of an electron into the 5d orbital needs 90000 cm^{-1} in the case of the free Gd^{3+} ion, such a transfer in the case

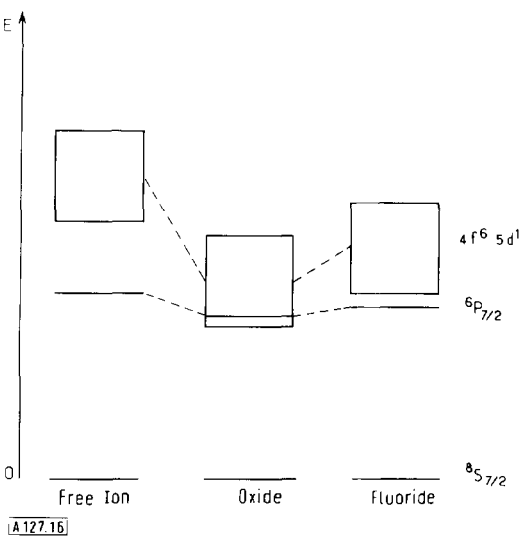

Fig. 16. Energy of the $^6P_{7/2}$ level in relation to the $4f^6 5d^1$ band in Eu^{2+}.

of divalent europium only requires 40000 cm^{-1}. Divalent europium contains seven f electrons, which corresponds to a high correlation energy as is the case for all half-occupied orbitals. As a result, a large energy difference separates the ground state $^8S_{7/2}$ of europium from the first excited level $^6P_{7/2}$ of the $4f^7$ configuration. This system can, therefore, lead to emission of ultraviolet radiation for which practical applications exist. However, this type of transition is not generally observ-

able, since the $5d^1$ levels are located above the $^6P_{7/2}$ level only in the free ion. In most compounds of europium, and especially in the oxides, these levels form a band and overlap with the excited states of the $4f^7$ configuration (Fig. 16). This band, corresponding to the 5d external orbitals, is very sensitive to the crystal field. Only in certain fluorides does it have a sufficiently high energy for the transition $^6P_{7/2}$-$^8S_{7/2}$ to appear. The emitted light is highly monochromatic and can be used either for developing lasers in the near UV or for xerography.

5. Conclusion

After his successful research on fluorine, *Moissan* queried: "Will fluorine never have any applications? It is very difficult to answer this question". History has answered in the affirmative: fluorine has become an industrially important element. In the field of materials, the applications of mineral fluorides are still relatively few and account for only small amounts. In pure research, however, these compounds attract considerable interest owing to their unusual and specific properties. No doubt this speculative work will lead to important applications in the future, some of which can already be discerned. But is that all that really matters? *Moissan* finished his commentary on the use of fluorine with this phrase: "In addition, I can say in all sincerity I was hardly thinking about it at the moment when I undertook this work, and I believe that all the chemists who have attempted such research before me were not thinking further of it: Scientific work is the search for truth".

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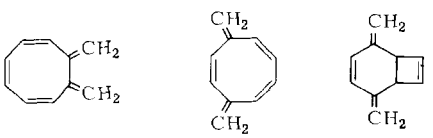
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying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

5,8-Bis(diphenylmethylene)-1,3,6-cyclooctatriene

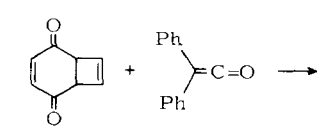
By *Yoshio Kitahara* (deceased), *Masaji Oda*, and *Yasutaka Kayama*[*]

Although 7,8-dimethylene-1,3,5-cyclooctatriene *(1)* has been prepared[1], 5,8-dimethylene-1,3,6-cyclooctatriene *(2)* is still unknown. An attractive synthetic approach to *(2)* consists in the thermal ring opening of its valence isomer 2,5-dimethylenebicyclo[4.2.0]oct-3,7-diene *(3)*.

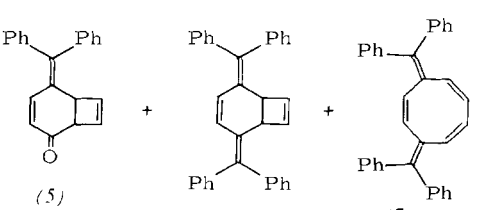


(1) *(2)* *(3)*

The reaction of diphenylketene with *p*-benzoquinone is known to afford diphenylquinomethane and tetraphenylquinodimethane[2]. In order to examine the feasibility of the above-mentioned route, we have prepared 2,5-bis(diphenylmethylene)bicyclo[4.2.0]oct-3,7-diene *(6)*, a valence isomer of 5,8-bis(diphenylmethylene)-1,3,6-cyclooctatriene *(7)*, by an analogous reaction from bicyclo[4.2.0]octa-3,7-diene-2,5-dione *(4)*[3]. The thermal isomerization of *(6)* to *(7)* proved highly successful.



(4)



(5) *(6)* *(7)*

Table 1. Physical data of *(5)*, *(6)*, and *(7)*.

(5): IR (liquid): $\nu_{max} = 1655\ cm^{-1}$ (C=O); ^{1}H-NMR ($CDCl_3$): $\delta = 3.61$ (1H, d, $J = 4.0$ Hz), 3.92 (1H, d, 4.0), 5.77 (1H, d, 10.2), 6.12 (2H, m), 6.9–7.4 ppm (11H, m)

(6): pale yellow prisms; m.p. 202–203 °C; ^{1}H-NMR ($CDCl_3$): $\delta = 3.76$ (2H, s), 6.15 (2H, s), 6.23 (2H, s), 7.17 ppm (20H, m); UV ($CHCl_3$): $\lambda_{max} = 276$ (sh, $\varepsilon = 11200$), 349 nm (34900)

(7): colorless needles: m.p. 181–182 °C; ^{1}H-NMR ($CDCl_3$): $\delta = 5.82$ and 6.02 (4H, A_2B_2), 6.11 (2H, s), 7.14 ppm (20H, m); UV ($CHCl_3$): $\lambda_{max} = 339$ nm ($\varepsilon = 26500$).

Reaction of *(4)* with diphenylketene (2.1 equiv.) in refluxing toluene for three days afforded, after silica gel column chromatography, *(5)*, *(6)*, and *(7)* in 35%, 24%, and 12% yield, respectively. Further reaction of *(5)* with diphenylketene afforded *(6)* and *(7)* in good yields (physical data summarized in Table 1).

The simultaneous formation of *(6)* and *(7)* indicates the thermal ring opening of the cyclobutene of *(6)* to be fairly easy. The rate constant at 144 °C in diphenyl ether is $1.23 \times 10^{-5}\ s^{-1}$, and the activation energy is 36.5 kcal/mol[4].

The absorption maximum of *(7)* is observed at 10 nm shorter wave length than that of *(6)* and the extinction coefficient of *(7)* is appreciably smaller. These observations suggest that while the six-membered ring of *(6)* is probably nearly planar owing to the rigidity of the molecule, the eight-membered ring of *(7)* is not planar, thus reducing the conjugation between the two diphenylmethylene groups through the ring.

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CAS Registry numbers:
(4), 54251-47-7; *(5)*, 59247-27-7; *(6)*, 59247-28-8; *(7)*, 59247-29-9; diphenylketene, 525-06-4

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[4] The kinetics was traced by means of ^{1}H-NMR in diphenyl ether using *tert*-butylbenzene as the internal standard, and the following Arrhenius equation was obtained: $\log k = 14.14 - (36500 \pm 2000)/2.303\,RT$.

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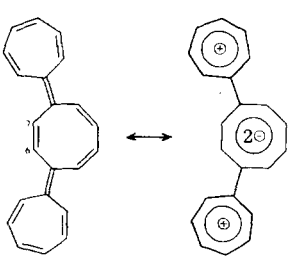
5,8-Bis(7-cycloheptatrienylidene)-1,3,6-cyclooctatriene

By *Yoshio Kitahara* (deceased), *Masaji Oda*, and *Hideo Miyazaki*[*]

It is of interest whether or not 5,8-bis(7-cycloheptatrienylidene)-1,3,6-cyclooctatriene *(1)* shows aromaticity arising from a contribution of the tripolar resonance form *(1')*.



(1) *(1')*

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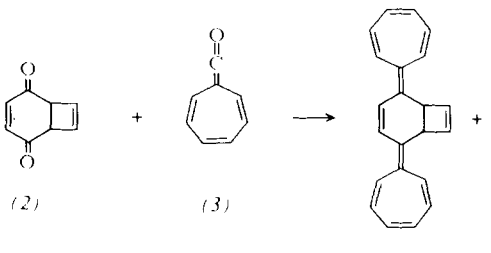
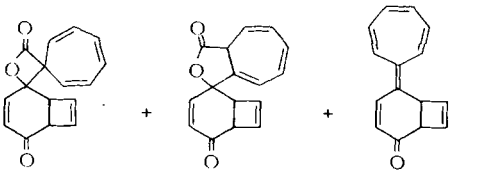
Sendai 980 (Japan)

The successful thermal isomerization of 2,5-bis(diphenylmethylene)bicyclo[4.2.0]oct-3,7-diene to 5,8-bis(diphenylmethylene)-1,3,6-cyclooctatriene[1] led us to attempt and to accomplish the synthesis of *(1)* along similar lines.

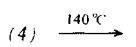
Reaction[2] of 2,5-dioxobicyclo[4.2.0]oct-3,7-diene *(2)*[3] with 7-carbonylcycloheptatriene *(3)*[4] (2.5 equiv.) generated *in situ* by the action of triethylamine on 1-cycloheptatrienecarbonyl chloride (benzene, room temperature, 16 h) afforded, after silica gel column chromatography and in the order of elution, 2,5-bis(7-cycloheptatrienylidene)bicyclo[4.2.0]oct-3,7-diene *(4)*, a β-lactone *(5)*, a mixture of γ-lactones differing in the positions of the double bond in the seven-membered ring [example: compound *(6)*], and a heptafulvene derivative *(7)* in 2.5 %, 32.1 %, 4.8 %, and 3.2 % yield, respectively[5]. While *(7)* is fairly stable at room temperature, *(4)* is extremely air-sensitive.



(2) *(3)* *(4)*



(5) *(6)* *(7)*



(4) *(1)*

When heated in refluxing benzene, *(5)* largely rearranged to *(6)* (64 %) and the desired decarboxylated product *(7)* was obtained in only 32 % yield. It was found, however, that silica gel in benzene effectively catalyzes quantitative decarboxylation of *(5)* to *(7)* at room temperature[5]. Reaction of *(7)* with *(3)* in refluxing benzene afforded *(4)* in 28 % yield. A simple preparation of *(4)* was achieved (18 % yield) by performing the reaction of *(2)* and *(3)* in refluxing benzene for ten minutes.

On heating a benzene solution of *(4)* at 140 °C in a sealed tube in which air had been rigorously replaced by nitrogen, the ^{1}H-NMR signal of the bridgehead protons of *(4)* at 3.74 ppm completely disappeared after 2 h. The desired compound *(1)* was obtained as a red-brown air-sensitive oil in 73 % yield by careful chromatography under nitrogen on a short silica gel column eluted with *n*-hexane.

Table 1. Physical data of *(1)* and *(4)*.

(1): red-brown oil: IR (liquid): ν_{max} = 3010, 1552, 1260, 727 cm^{-1}; UV (cyclohexane): λ_{max} = 226 (ε = 18600), 414 nm (15100); ^{1}H-NMR (C_6D_6, 100 MHz): δ = 5.5–6.3 ppm [m, including a singlet at 6.16 ppm (*ca.* 2H; H-6, H-7)]. *(4)*: dark red-brown needles; m.p. 148–149 °C (sealed tube); IR (KBr): ν_{max} = 3020, 1559, 730 cm^{-1}; UV (CH_2Cl_2): λ_{max} = 237 (ε = 22400), 434 nm (43600); ^{1}H-NMR ($CDCl_3$): δ = 3.74 (2H, s; H-1, H-6), 5.43–6.45 (12H, m), 6.16 (2H, s), 6.38 ppm (2H, s).

The physical data of *(1)* and *(4)* are listed in Table 1. The ^{1}H-NMR data indicate that *(1)* is a nonaromatic compound. The UV spectra of *(1)* and *(4)* resemble those of the diphenylmethylene analogs[1]. Accordingly, the eight-membered ring of *(1)* may not be planar.

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(1), 7443-79-0; *(2)*, 54251-47-7; *(3)*, 36374-18-2; *(4)*, 59247-43-7; *(5)*, 59247-44-8; *(6)*, 59247-45-9; *(7)*, 59247-46-0

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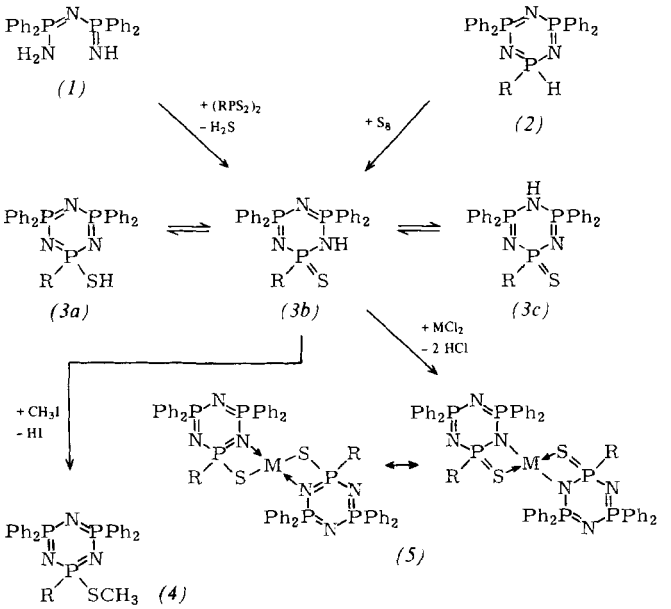
[5] The yields of compounds isolated, particularly *(5)* and *(7)*, varied with the chromatographic conditions.

Bis[cyclotri(λ^5-phosphazane)dienethionato]-Ni^{II}, -Pd^{II} and -Pt^{II} Complexes and Their Structure[1]

By *Alfred Schmidpeter, Klaus Blanck,* and *Farid R. Ahmed*[*]

Dedicated to Professor Egon Wiberg on the occasion of his 75th birthday

Cyclotri(λ^5-phosphazane)diene-2-thiones *(3)* are accessible by cyclization[2] of aminodi(λ^5-phosphazene)s *(1)* with perthiophosphonic anhydrides and—as reported here—also by sulfurization of hydridocyclotri(λ^5-phosphazene)s *(2)*. They are present in solution as tautomer *(3b)*, their methyl derivatives *(4)* on the other hand derive from the other tautomer *(3a)*[2]. This follows from the inequivalence and equivalence, respectively, of P^4 and P^6, and from the doublet-splitting of the ^{1}H-NMR signal of the introduced methyl group (Table 1).



(1) *(2)* *(3a)* *(3b)* *(3c)* *(5)* *(4)*

In the form of their anions, compounds *(3)* react with Ni, Pd, and Pt dichlorides to give the bis(thionato)metal(II) complexes *(5)*. The ^{31}P-NMR spectra of *(5)* (Table 1) relate

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Table 1. Properties and NMR data [a] of 4,4,6,6-tetraphenylcyclotri(λ⁵-phosphazane)dienethione derivatives.

		R = CH_3					R = $CH_3OC_6H_4$					R = C_6H_5O				
	M	M.p. [°C]	J_{PSCH} [Hz] Color	δP^2	δP^4	δP^6	M.p. [°C]	J_{PSCH} [Hz] Color	δP^2	δP^4	δP^6	M.p. [°C]	J_{PSCH} [Hz] Color	δP^2	δP^4	δP^6
(3)		216		49.5	13.5	19.2	183—185 [2]		45.2	15.2	21.2	227—228		44.3	15.7	22.6
(4)		109	13.1	38.6	14.1		129—130 [2]	13.6	27.0	14.1		157—158	16.2	30.9	15.2	
(5)	Ni	302	violet		[b]		241	turquoise	60.6	16.5	26.6	241	lavender		[b]	
(5)	Pd	303—304	orange-brown		[b]		283—284	red-brown	48.7	10.9	26.2	249	red-brown	49.0	11.9	27.9
(5)	Pt	281—282	light-yellow	57.9	9.1	27.1						186	light-yellow	52.9	10.4	28.1

[a] Solvent: nitrobenzene; δ values in ppm against H_3PO_4, external.
[b] Solubility too low.

well with those of *(3b)* and, in particular, show P^4 and P^6 once again as nonequivalent. Thus they show that the phosphazene ring is coordinated to the metal atom *via* N^1, and suggest a four-ring chelate derivable from *(3a, b)*, which however, can be constructed only if the generally observed geometry of the participating structural elements is partially altered.

The structure of *(5)*, R = CH_3, M = Ni, was determined X-ray crystallographically by the heavy atom method[3] and refined to $R = 0.041$ and $R_w = 0.040$: space group $P\bar{1}$; $a = 11.142$, $b = 12.598$, $c = 9.620$ Å; $\alpha = 110.82$, $\beta = 77.84$, $\gamma = 102.58°$; $Z = 1$; $d_{calc} = 1.416$, $d_{exp} = 1.415\ g\ cm^{-3}$. The nickel atom forms a crystallographic center of inversion and is surrounded by a rigidly planar array of two sulfur atoms and two nitrogen atoms *i.e.* a sulfur and a geminal nitrogen from each of the two ligands. Both chelate rings are folded along the N^1S diagonals through 25.4°, as required on grounds of symmetry, in opposite directions.

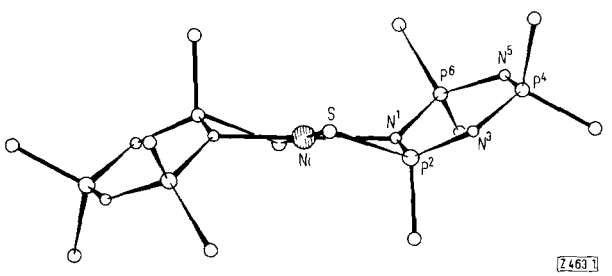

Fig. 1. Molecular structure of the bischelate *(5)*, R = CH_3, M = Ni. Of the eight phenyl groups only the *P*-bonded carbon atoms are shown.

Chelate formation becomes possible because a) the phosphazene nitrogen coordinated to Ni is not planar[4] and is in a very unsymmetrical environment (angle $P^2N^1P^6$ 123.0, P^6N^1Ni 130.2, P^2N^1Ni 95.4°; sum of angles 348.6°), b) its bonds in the ring (N^1—P^2 1.649, N^1—P^6 1.635 Å) are longer than the other PN bonds (1.581—1.591 Å), and c) at P^2 the ligand plane is not perpendicular to the phosphazene plane (dihedral angle 82.5°, while in other cases it deviates by at most 5° from a right angle).

Cyclotri(λ⁵-phosphazane)diene-2-thione (3)

A solution of hydridocyclotri(λ⁵-phosphazene) *(2)* in methylene chloride is treated with a stoichiometric amount of sulfur and heated to boiling. After *ca.* 10 min the sulfur has dissolved, and *(3)* separates out as fine crystals (yield 90—95 %).

Methylthiocyclotri(λ⁵-phosphazene) (4)

1 mmol of *(3)* dissolves after several hours stirring in a solution of 10 ml methylene chloride and 3 ml CH_3I. Evaporation of the solution affords *(4)*-hydroiodide as a solid residue, from which *(4)* is obtainable by recrystallization from acetonitrile/water (1 : 1) (yield 82—88 %).

Cyclotri(λ⁵-phosphazane)dienethionato complexes (5)

To a solution of *(3)* (2 mmol) and sodium methoxide (2 mmol) in methanol (10 ml) is added 1 mmol $NiCl_2(H_2O)_6$ (dissolved in 5 ml of methanol) or $PdCl_2$ (dissolved in 25 ml of acetonitrile) or $(C_6H_5CN)_2PtCl_2$ (dissolved in 10 ml of acetonitrile). A finely crystalline precipitate of *(5)* is formed; in the first and second case immediately, in the third case after 10 minutes' boiling and subsequent cooling. *(5)* is recrystallized from nitrobenzene (yield 80—95 %).

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CAS Registry numbers:
(2), R = CH_3, 18033-98-2; *(2)*, R = $CH_3OC_6H_4$, 59562-83-3; *(2)*, R = C_6H_5O, 18033-97-1; *(3)*, R = CH_3, 59562-84-4; *(3)*, R = $CH_3OC_6H_4$, 22779-75-5; *(3)*, R = C_6H_5O, 59562-85-5; *(4)*, R = CH_3, 59562-86-6; *(4)*, R = $CH_3OC_6H_4$, 22779-79-9; *(4)*, R = C_6H_5O, 59562-87-7; *(5)*, M = Ni, R = CH_3, 59671-82-8; *(5)*, M = Ni, R = $CH_3OC_6H_4$, 59671-83-9; *(5)*, M = Ni, R = C_6H_5O, 59671-84-0; *(5)*, M = Pd, R = CH_3, 59671-85-1; *(5)*, M = Pd, R = $CH_3OC_6H_4$, 59697-10-8; *(5)*, M = Pd, R = C_6H_5O, 59671-86-2; *(5)*, M = Pt, R = CH_3, 59671-87-3; *(5)*, M = Pt, R = C_6H_5O, 59671-88-4; CH_3I, 74-88-4; S_8, 10544-50-0; ^{31}P, 7723-14-0

[1] Phosphazenes, Part 56. This work was supported by the Fonds der Chemischen Industrie.—Part 55: *A. Schmidpeter* and *H. Eiletz*, Chem. Ber. *109*, 2340 (1976).
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Three-Component Reactions with Aryl Isothiocyanates. Synthesis of 5-Arylimino-1,2,4-thiadiazolidin-3-ones

By *Gerrit L'abbé* and *Gabriël Verhelst*[*]

The use of isothiocyanates in a three-component synthesis of heterocycles is scarcely documented in the literature[1]. In this report we describe a novel synthesis of substituted 5-imino-1,2,4-thiadiazolidin-3-ones which have been prepared previously from isothiocyanates in a three-step procedure[2].

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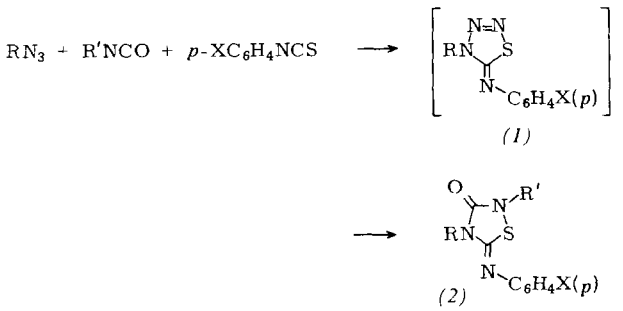
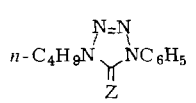


According to our method the heterocycles *(2)* are obtained in high yields (see Table 1) when alkyl azides, aryl isothiocyanates, and alkyl or aryl isocyanates are mixed together under well-defined conditions (see procedure). Structure assignment of the heterocycles *(2)* was based mainly on IR spectra [KBr, $\nu(C{=}O) \approx 1710$, $\nu(C{=}N) \approx 1630\,cm^{-1}$] and on the ^{13}C-NMR spectra[3].

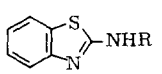
Table 1. Products *(2a)* to *(2d)* of the three-component reaction and compound *(2e)* obtained from *(1e)*. The yields of *(2a)* to *(2d)* are based on the isocyanate.

Cpd.	R	R'	X	Yield [%]	M.p. [°C]
(2a)	$c\text{-}C_6H_{11}$	$n\text{-}C_4H_9$	Cl	84	66—67 (Hexane)
(2b) [a]	$n\text{-}C_4H_9$	C_6H_5	CH_3	82	96—97 (Hexane)
(2c) [b]	$C_6H_5CH_2$	$n\text{-}C_4H_9$	H	60	75—76 (Hexane/ether)
(2d) [c]	$n\text{-}C_4H_9$	$n\text{-}C_4H_9$	H	73	[d]
(2e)	CH_3	$n\text{-}C_4H_9$	H	95	[e]

[a] Plus compound *(3a)*.
[b] Plus compound *(4a)*.
[c] Plus compounds *(3b)* and *(4b)*.
[d] B.p. 165°C/1 torr; $n_D^{21} = 1.5555$.
[e] $n_D^{25} = 1.5800$.

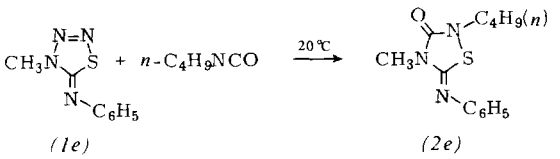


(3a), Z = O
(3b), Z = S



(4a), R = $C_6H_5CH_2$
(4b), R = $n\text{-}C_4H_9$

Mechanistically, the reactions seem to proceed *via* the intermediacy of an iminothiatriazoline *(1)* for several reasons: (i) alkyl azides are known to be thermally stable under the reaction conditions[4], thus excluding a nitrene mechanism; (ii) alkyl azides are also unreactive towards most isocyanates[5], and the tetrazolin-5-one *(3a)* was isolated in only one case as a side product (see Table 1); and (iii) addition of alkyl azides to the C=N bond of isothiocyanates would give 1,4-disubstituted tetrazoline-5-thiones which are, however, thermally stable[6]; the tetrazoline-5-thione *(3b)* was isolated as minor product in only one case (see Table 1). To test our mechanistic interpretation, 4-methyl-5-phenylimino-1,2,3,4-thiatriazoline *(1e)* was synthesized by the method of *Neidlein* and *Tauber*[7]. This compound proved to be thermally stable up to 110°C, at which temperature it decomposed into 2-methylaminobenzothiazole [the 2-aminobenzothiazoles *(4a)* and *(4b)* are formed as by-products on synthesis of *(2c)* and *(2d)*]. In the presence of butyl isocyanate, however, an exothermic reaction already occurs at room temperature and furnishes *(2e)* in 95 % yield. This experiment substantiates the proposed



(1e) *(2e)*

mechanism and clearly points to a bimolecular mechanism in the second stage of the reaction.

General procedure:

To a solution of alkyl azide (0.08 mol) and isocyanate (0.04 mol) at 80°C isothiocyanate (0.02 mol) was added in portions over a period of seven days. Then the excess of azide and heterocumulenes was distilled off *in vacuo* and the residual oil was purified by column chromatography on silica gel using ether/hexane (20:80) as the eluent.

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(2a), 59574-46-8; *(2b)*, 59574-47-9; *(2c)*, 59574-48-0; *(2d)*, 59574-49-1; *(2e)*, 59574-50-4; cyclohexyl azide, 19573-22-9; butyl azide, 7332-00-5; benzyl azide, 622-79-7; methyl azide, 624-90-8; *p*-chlorophenyl isothiocyanate, 2131-55-7; *p*-tolyl isothiocyanate, 622-59-3; phenyl isothiocyanate, 103-72-0; butyl isocyanate, 111-36-4; phenyl isocyanate, 103-71-9

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Solvolysis of the Hexafluorophosphate Ion and the Structure of [Tris(μ-difluorophosphato)bis(pentamethylcyclopentadienylrhodium)] Hexafluorophosphate[**]

By *Stephen J. Thompson*, *Pamela M. Bailey*, *Colin White*, and *Peter M. Maitlis*[*]

We report here on the preparation and some properties of the novel dicationic solvate complexes *(2)* and on the observation of the solvolysis of the hexafluorophosphate counterion to give difluorophosphate, which has been characterized as a ligand in the complex *(3)*. In view of the ease with which this reaction occurs care in the use of PF_6^-, and similar counterions previously thought to be inert, is necessary.

The solvate complexes *(2)* were obtained from the dichloro(pentamethylcyclopentadienyl)rhodium or -iridium compounds[1] *(1)* by reaction with $AgPF_6$ in the solvent (solv.). Those with solv. = acetonitrile, pyridine or dimethyl sulfoxide (DMSO) could be isolated but those with solv. = acetone, methanol or dichloromethane could only be obtained

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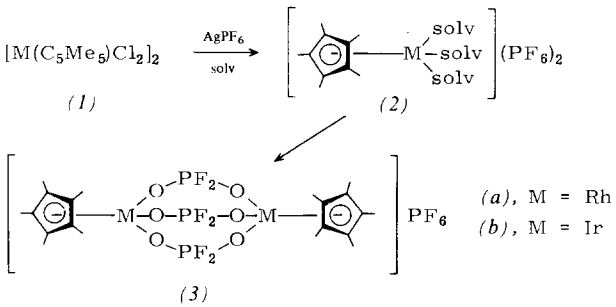
in solution. These complexes react readily with a variety of organic ligands (*e.g.* arenes) to give complexes such as $[M(C_5Me_5)(arene)]^{2+}$.

The rhodium-DMSO complex was shown by its IR spectra to be *O*-bonded to the metal both in the solid (Nujol mull) and in acetone solution [ν(SO) 953 cm^{-1}], but the iridium-DMSO complex was both *O*- and *S*-bonded in the solid [ν(SO) 901, 1135 cm^{-1} in Nujol mull] and only *S*-bonded in acetone solution [ν(SO) 1128 cm^{-1}][2]. These observations suggest that ($Rh^{III}C_5Me_5$) is a "harder" coordination center than ($Ir^{III}C_5Me_5$).



When attempts were made to isolate complex *(2a)*, solv.= Me_2CO, or when the acetone solution was heated (50 °C/12 h), a complex decomposition reaction occurred to give complex *(3a)* which contained bridging PO_2F_2 ligands. This was shown by NMR and IR spectroscopy, by an X-ray structure determination of a crystal of *(3a)* (figure) and by direct synthesis from *(2a)* and HPO_2F_2.

The ^{31}P-NMR spectrum (w.r.t. 85 % H_3PO_4 ext.) of *(3a)* showed a septet due to the PF_6^--anion [$\delta = -166.2$ ppm, $J_{PF} = 708$ Hz] and a triplet due to the PO_2F_2 ligands [$\delta = -33.1$ ppm, $J_{PF} = 952$ Hz] in the ratio of 1:3. The ^{19}F-NMR spectrum (w.r.t. CF_3CO_2H ext.) showed two doublets [$\delta = -5.7$ and $+3.4$ ppm] in a 1:1 ratio, while the ^{1}H-NMR spectrum showed a singlet ($\delta = 1.65$) arising from the ten equivalent methyl groups.

The salt $[C_{20}H_{30}F_6O_6P_3Rh_2]F_6P$, $M = 924.14$, crystallizes monoclinically with $a = 10.186(5)$, $b = 37.68(2)$, $c = 12.82(2)$ Å, $\beta = 98.06(1)°$; $V = 4872$ Å^3; $d_{calc} = 1.889$, $d_{obs} = 1.83$ g/cm^3; $Z = 6$; space group $P2_1$. Three-dimensional X-ray data with $6.5° \leq 2\theta \leq 50°$ were collected with the crystal mounted along the *c* axis on a Stoe STADI 2 diffractometer, using graphite monochromated $Mo_{K\alpha}$ radiation. 4210 independent reflections had $I_{obs} \geq 3\sigma(I_{obs})$. The positions of the six independent rhodium atoms were determined by Patterson superposition methods, and the remaining non-hydrogen atoms found from difference Fourier syntheses. Block diagonal least-squares refinement with constrained geometries for the pentamethylcyclopentadienyl groups reduced *R* to 0.112, at which point a difference Fourier synthesis indicated some of the fluorine atoms to be disordered; this is currently under further investigation. It is not possible to distinguish the O and F atoms of the PO_2F_2 ligands and their formulation as *O*-bonded to Rh rests largely on the ^{19}F-NMR spectrum which shows only one doublet, arising from coupling to ^{31}P, down to -90 °C. A PO_2F_2 ligand which was *O*- and *F*-, or only *F*-bonded to Rh would show different spectroscopic behavior, in particular a coupling to ^{103}Rh (100 %, $I = \frac{1}{2}$).

The hexafluorophosphate ion is normally regarded as extremely stable; it only undergoes very slow hydrolysis in 6 M HCl at 45 °C to phosphate[3] and hydrolysis under alkaline conditions is even slower and again phosphate is the product[4, 5]. Metal ion catalysis has been observed both under acid [by Th^{IV} or Zr^{IV}][6] and under alkaline [by the larger

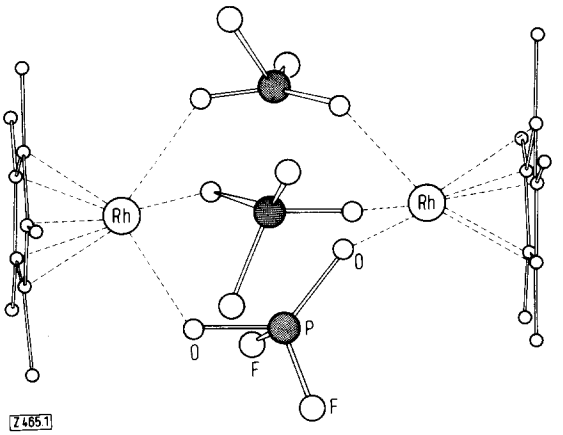


Fig. 1. Structure of the complex cation $[C_5Me_5Rh(PO_2F_2)_3RhC_5Me_5]^+$ in *(3a)*.

alkali-metal ions][5] conditions. In the Al^{III}-catalyzed reactions at low acidity kinetic evidence for the build-up of an intermediate has been given[6] but the present work describes the first defined example of the partial solvolysis of the PF_6^- ion to the $PO_2F_2^-$ ion as well as the first structure determination of a transition metal difluorophosphate complex. It is also noteworthy that the PO_2F_2 ligands bridge two rhodium atoms[7]. The iridium complex *(3b)* was formed analogously from $[Ir(C_5Me_5)(Me_2CO)_3](PF_6)_2$ but it reacted further[8]. Addition of water did not significantly increase the rate of formation of *(3a)* but addition of mesityl oxide caused a substantial acceleration.

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(1a), 12354-85-7; *(1b)*, 12354-84-6; *(2a)*, solv.=acetonitrile, 59738-28-2; *(2a)*, solv.=pyridine, 59738-30-6; *(2a)*, solv.=dimethyl sulfoxide, 36222-86-3; *(2b)*, solv.=acetonitrile, 59738-32-8; *(2b)*, solv.=pyridine, 59738-34-0; *(2b)*, solv.=dimethyl sulfoxide, 59738-06-6; *(3a)*, 59738-36-2; *(3b)*, 59738-46-4; PF_6^-, 16919-18-9

[1] See for example, *J. W. Kang, K. Moseley*, and *P. M. Maitlis*, J. Am. Chem. Soc. *91*, 5570 (1969); *P. M. Maitlis*, Trans. N. Y. Acad. Sci. *33*, 87 (1971); *C. White* and *P. M. Maitlis*, J. Chem. Soc. *A 1971*, 3322.
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[5] *I. G. Ryss* and *V. B. Tul'chinskii*, Zhur. Neorg. Khim. *9*, 836 (1967).
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[8] *S. J. Thompson, C. White*, and *P. M. Maitlis*, unpublished results.

The $H_5O_2^+$ Ion in Hydrogen Bromide Dihydrate[***]

By *Rainer Attig* and *Jack M. Williams*[*]

Accurate measurement of the hydrated proton $[H(H_2O)_n]^+$ in the solid state by neutron diffraction has so far been limited to hydrates of strong organic acids[1] or acid metal com-

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plexes[2]. According to X-ray crystallographic and spectroscopic findings the crystalline hydrates of the mineral acids may also be formulated as oxonium salts; but their low melting points make it difficult to prepare single crystals large enough for neutron diffraction experiments.

We have now succeeded in preparing a single crystal of hydrogen bromide dihydrate $HBr \cdot 2H_2O$ weighing *ca.* 130 mg in a lead-glass capillary by controlled passage of a hot-wire loop along the capillary in a stream of cold gas[3]. The positions of the O and Br atoms were already known from an earlier X-ray structure analysis[4], from which the probable presence of $H_5O_2^+$ and Br^- ions was concluded. Our neutron diffraction analysis has not only made it possible to confirm the location of the O and Br atoms but also of the H atoms, and to measure the $H_5O_2^+$ ion exactly.

H_5O_2Br crystallizes monoclinically in the space group $P2_1/c$ with the lattice constants (−40°C) $a=4.23$, $b=12.57$, $c=6.94$ Å; $\beta=101.4°$; $Z=4$; d_{exp} (−15°C) = 2.11[5], $d_{calc}=2.15\ g\,cm^{-3}$. Three-dimensional neutron diffraction data were collected with the help of the CP5 reactor at the Argonne National Laboratory. Structure determination based on the positions of the Br and O atoms found by X-ray studies, as well as isotropic and anisotropic refinement for all atoms with 522 independent data corrected for absorption ($\mu=1.62\ cm^{-1}$) with maximum diffraction angle $2\theta=80°$ ($\lambda_n=1.142$ Å) gave an agreement factor of $R=0.149$ (0.094 for 373 reflections $>1\sigma$). The resulting positions of the atoms are listed in Table 1.

Table 1. Atomic coordinates of H_5O_2Br (in brackets: estimated standard deviation to the last decimal place).

	x	y	z
Br	0.0244(9)	0.3314(3)	0.1553(5)
O(1)	0.5622(16)	0.1253(4)	0.0421(10)
O(2)	0.3037(18)	0.0599(6)	0.2964(10)
H(1)	0.4271(22)	0.0966(6)	0.1657(14)
H(11)	0.7041(24)	0.1872(8)	0.0791(15)
H(12)	0.4026(28)	0.1433(7)	−0.0774(16)
H(21)	0.2223(25)	−0.0115(8)	0.3016(13)
H(22)	0.2321(25)	0.1023(7)	0.3972(15)

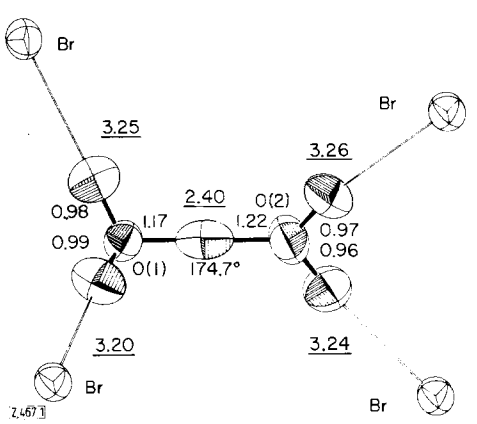

Fig. 1. The cation H_5O_2 in hydrogen bromide dihydrate. Atomic distances in Å, underlined values for distances between O and Br atoms; standard deviation 0.01 Å (for the quoted angle 0.8°).

Figure 1 shows the diaquahydrogen cation with four symmetry equivalent bromide ions as hydrogen bridging partners. The central O—H—O bridge is remarkably short (mean value of previously determined O—O distances in cations of this type amounts to 2.44 Å). The hydrogen atom is not exactly central, even in this short bridge, a finding that can be correlated with the slight asymmetrical environment of the two oxygen atoms in view of the bond lengths and O—Br contacts. A deviation of about 5° from the straight O—H—O arrangement was previously observed in all $H_5O_2^+$ ions, which are not fixed at 180° by a center of symmetry.

In contrast to the terminal hydrogen atoms, the central atom shows its largest vibration amplitude almost in the bond direction—a finding which in similar cases was explained in terms of a broad, flat potential well[6]. There is no evidence of disorder of the hydrogen atom between two half-occupied sites.

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CAS Registry number:
H_5O_2Br, 51222-77-6

[1] *J. M. Williams* and *S. W. Peterson*, Acta Crystallogr. *A 25*, S113 (1969); *J.-O. Lundgren* and *J. M. Williams*, J. Chem. Phys. *58*, 788 (1973); *J.-O. Lundgren* and *R. Tellgren*, Acta Crystallogr. *B 30*, 1937 (1974).
[2] *J. M. Williams* and *S. W. Peterson*, J. Am. Chem. Soc. *91*, 776 (1969); *G. D. Brunton* and *C. K. Johnson*, J. Chem. Phys. *62*, 3797 (1975).
[3] Samples with a molar ratio of exactly 1:2 were prepared by Prof. *J. E. Finholt*, Carlton College, Northfield, Minn. (USA).
[4] *J.-O. Lundgren*, Acta Crystallogr. *B 26*, 1893 (1970).
[5] *H. W. B. Roozeboom*, Recl. Trav. Chim. Pays-Bas *4*, 344 (1885).
[6] *A. Sequeira*, *C. A. Berkebile*, and *W. C. Hamilton*, J. Mol. Struct. *1*, 283 (1967—1968); *A. L. Macdonald*, *J. C. Speakman*, and *D. Hadzi*, J. Chem. Soc. Perkin II *1972*, 825.

Recovery of Chiral α-Ferrocenylalkylamines on Stereoselective Peptide Synthesis by Four-Component Condensation[**]

By *Gerhard Eberle* and *Ivar Ugi*[*]

α-Ferrocenylalkylamines *(4)* have proved well suited as chiral amine components for stereoselective peptide syntheses by four-component condensation[1]. In combination with the recently discovered multiplication of stereoselectivity[2] and the enhancement of stereoselectivity by addition of quaternary ammonium salts of the acid component *(3)*[3] products *(5)* [and *(7)*] of almost uniform stereochemistry can be obtained by use of the amines *(4)*, and especially α-ferrocenylisobutylamine *(4b)*[1,2] (Scheme 1).

Conventional methods of removing the chiral ferrocenylalkyl group from the condensation product *(5)*[1,2] have not hitherto permitted recovery of the chiral amine *(4)*. This is a considerable drawback since the amines *(4)* are usually only preparable with great difficulty[1].

Ratajczak and *Misterkiewicz* recently reported[4] that α-ferrocenylethanol *(9a)* reacts with thioglycolic acid *(6)* in the presence of trifluoroacetic acid to form *(8a)*, and that *(9a)* is accessible from *(8a)* by hydrolysis in the presence of $HgCl_2$, the reaction *(8a)* → *(9a)* belonging to the retentive S_N1 type[5].

We have now found that *N*-(α-ferrocenylalkyl)-peptide derivatives *(5)* are smoothly cleaved by *(6)* in the presence of trifluoroacetic acid into *(7)* and *(8)*, with complete retention of configuration at the chiral center bearing the ferrocenyl ligand.

For instance, treatment of the tripeptide derivative *(5c)*[6] at room temperature in 0.05 M acetone solution with an excess

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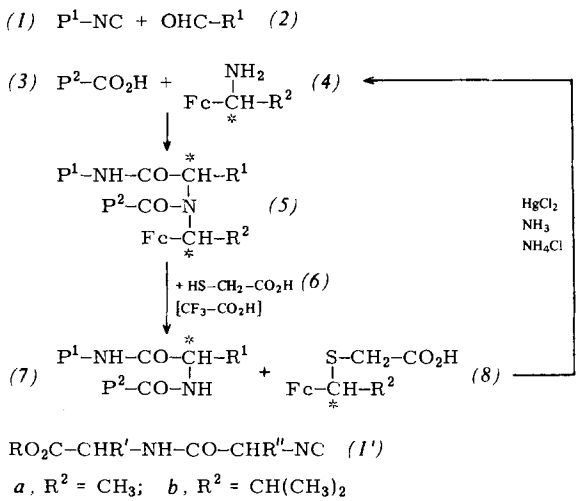
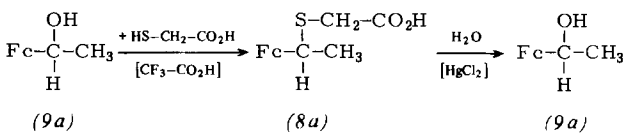
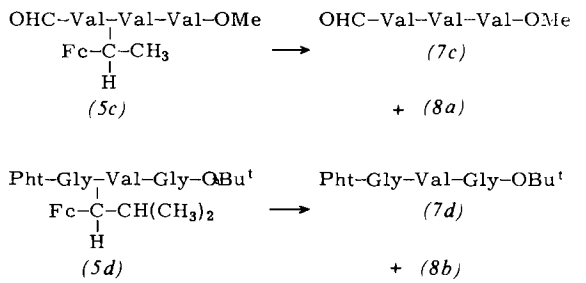


Scheme 1. Stereoselective synthesis of the peptide derivatives *(5)* by four-component condensation of compounds *(1)* to *(4)*, cleavage of *(5)* with thioglycolic acid in the presence of trifluoroacetic acid to give the peptides *(7)* and (α-ferrocenylalkylthio)acetic acids *(8)* and recovery of the chiral starting component *(4)*. *(1)* is an isocyanide derived from an α-amino acid or peptide ester, preferably an *N*-(α-isocyanoacyl)-α-amino acid ester *(1')*. *(2)* is an α-amino aldehyde OHC—CHR—NH_2 and *(3)* is an α-amino acid or a peptide with an N-terminal protective group. Fc = ferrocenyl.

of thioglycolic acid *(6)* and a catalytic amount of trifluoroacetic acid over 24 h affords a 94 % yield of the cleavage products *(8a)* and *(7c)*.—Reaction of *(5d)*[6] in trifluoroacetic acid with thioglycolic acid *(6)* for 48 h furnishes *(8b)* and *(7d)* in 87 % yield.



The *S*-(α-ferrocenylalkyl)thioglycolic acids *(8a)*,*(8b)* thus obtained are optically pure, as demonstrated by comparison with literature data and by further reaction to the amines *(4)*. Dissolution of *(R)*-*(8a)* or *(R)*-*(8b)* in concentrated ammonia and addition of NH_4Cl and $HgCl_2$ (molar ratio 1:2:2) affords, after reaction for 7 to 9 h at 25 °C, *(4a)* in 78 % yield and *(4b)* in 73 % yield, respectively. Both amines *(4)* are 98 to 99 % optically pure.



The readily accessible racemic *S*-(α-ferrocenylalkyl)thioglycolic acids *(8a)*,*(8b)* can be enantiomerized with the aid of (−)-ephedrine[4] and (−)-pseudoephedrine, thus transforming the reaction *(8)* → *(4)* into a new productive approach to chiral α-ferrocenylalkylamines *(4)*.

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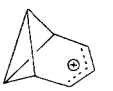
CAS Registry numbers:
(4a), 59685-04-0; *(4b)*, 54053-41-7; *(5c)*, 59643-30-0; *(5d)*, 59643-31-1; *(6)*, 68-11-1; *(7c)*, 59620-86-9; *(7d)*, 3442-63-5; *(8a)*, 56498-34-1; *(8b)*, 59643-32-2

[1] *I. Ugi et al.* in *Y. Wolman:* Peptides 1974. Wiley, New York and Israel University Press, Jerusalem, 1975, p. 71, and references cited therein.
[2] *R. Urban* and *I. Ugi*, Angew. Chem. *87*, 67 (1975); Angew. Chem. Int. Ed. Engl. *14*, 61 (1975).
[3] *D. Rehn, D. Marquarding*, and *I. Ugi*, to be published; *I. Ugi, K. Offermann, H. Herlinger*, and *D. Marquarding*, Justus Liebigs Ann. Chem. *709*, 1 (1967); *I. Ugi* and *G. Kaufhold*, *ibid.* *709*, 11 (1967).
[4] *A. Ratajczak* and *B. Misterkiewicz*, J. Organomet. Chem. *91*, 73 (1975).
[5] *G. Gokel* and *I. Ugi*, Angew. Chem. *83*, 178 (1971); Angew. Chem. Int. Ed. Engl. *10*, 191 (1971); *G. Gokel, D. Marquarding*, and *I. Ugi*, J. Org. Chem. *37*, 3052 (1972).
[6] For preparation of these compounds by four-component condensation: *D. Marquarding, D. Rehn, I. Ugi*, and *R. Urban*, to be published.

Tricyclo[4.1.0.$0^{2,7}$]heptenyl Cation—A New Isomer of the Tropylium Ion[**]

By *Manfred Christl* and *Gertrud Freitag*[*]

Carbocations having the molecular formula $C_7H_7^{\oplus}$ have been studied in great detail[1], not least because of the theoretical interest attracted by the bonding in the tropylium ion and the 7-norbornadienyl cation. Although a member of this family, the tricyclo[4.1.0.$0^{2,7}$]heptenyl cation *(1)* has so far remained unknown[1b]. We now wish to report a facile entry to this system and its rearrangement.



(1)

On standing for 15 h at 80 °C in an inert solvent such as tetrachloromethane, 7,7-dibromotetracyclo[4.1.0.$0^{2,4}$.$0^{3,5}$]-heptane *(2)* is smoothly transformed into 4,5-dibromotricyclo[4.1.0.$0^{2,7}$]hept-3-ene *(3)*[2], thus providing some indication of the considerable stability of the 4-bromotricycloheptenyl cation *(4)*. Departure of the *endo* bromine as an anion and disrotatory ring opening of the 1,6-bond in *(2)* lead directly to *(4)*, which is trapped by the bromide ion to form *(3)*. In 50 % aqueous acetone containing triethylamine compound *(2)* is no longer stable at room temperature. The polar solvent facilitates ionization to give *(4)* which, on reaction with water as nucleophile, furnishes the alcohol *(5)*[3], b.p. 40—60 °C (bath)/0.01 torr, m.p. 62—65 °C. Compound *(5)* is also accessible from *(3)* in 60—70 % yield by solvolysis in tetrahydrofuran/water or acetone/water mixtures containing triethylamine at room temperature. On treatment with sodium in liquid ammonia at −70 °C *(5)* is converted in *ca.* 60 % yield into the bromine-free species tricyclo[4.1.0.$0^{2,7}$]hept-4-en-3-ol *(6)*[3], b.p. 75—78 °C/15 torr, m.p. 16—19 °C, which has recently been synthesized *via* another route[4].

The 3,5-dinitrobenzoates are accessible from *(5)* and *(6)* in the usual way by treatment with 3,5-dinitrobenzoyl chloride. Entirely as would be expected from the solvolysis behavior of *(3)*, 6 hours' refluxing of *(5)*-dinitrobenzoate[3], m.p. 122—124 °C, in 65 % aqueous acetone in the presence of diisopropylethylamine merely afforded a 65 % yield of *(5)*. In contrast,

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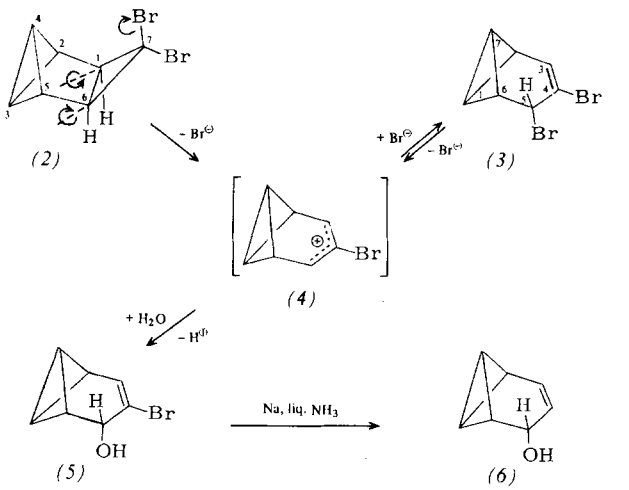
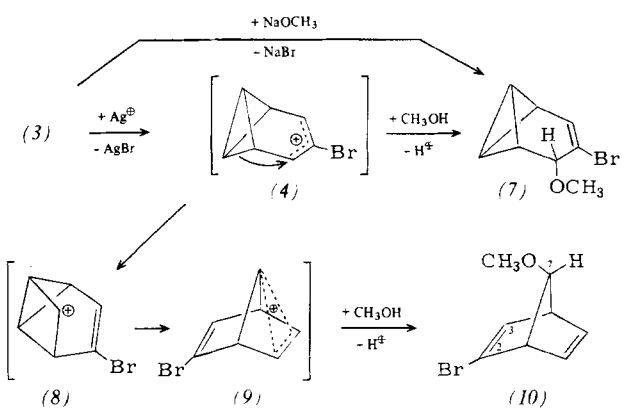
solvolysis of *(6)*-dinitrobenzoate[3], m.p. 94°C, in the same medium for 3 h at 70°C gave a 7:3 mixture of *(6)* and di-2,4,6-cycloheptatrienyl ether. We suspect intermediate formation of *(1)* which rearranges to 7-norbornadienyl cation and thus with water furnishes 7-norbornadienol (see below). The facile conversion of the latter into di-2,4,6-cycloheptatrienyl ether in aqueous alkaline solution has recently been reported[5].



A better insight into the rearrangement is provided by cation *(4)* in a less nucleophilic medium. Dropwise addition of a benzene solution of silver perchlorate at room temperature to a solution of *(3)* in a 15:4:2 mixture of ether, methanol, and triethylamine[6] immediately precipitates silver bromide and a 60% yield of 4-bromo-5-methoxytricyclo[4.1.0.0^{2,7}]-hept-3-ene *(7)* and 2-bromo-*syn*-7-methoxynorbornadiene *(10)* in the ratio 88:12 is isolated. Mixing of toluene solutions of *(3)* and silver perchlorate at 20 or −70°C and subsequent addition of methanol furnishes a 60% yield of *(10)*[3], b.p. 95—105°C (bath)/14 torr, as sole product. The stereochemistry at C-7 follows from the 1.1-Hz coupling constant between H-7 and H-3[7]. *(7)*[3], b.p. 44—45°C/0.04 torr, is formed in 95% yield from *(3)* with sodium methoxide in methanol.



It is improbable that the rearrangement of the cation *(4)* is affected by silver(I) ions since they even fail to attack the neutral species *(7)* under the conditions of the reaction. The transition to the 7-norbornadiene system is most simply explained by a 1,2 shift of one of the four peripheral bicyclobutane bonds to the adjacent cationic center. Thus *(4)* affords *(8)*, 2-bromo-7-norbornadienyl cation in one of the classical formulations[1c]. *(9)* corresponds to the generally accepted bishomocyclopropenyl structure[1]. Approach of the nucleophile methanol from the side of the free double bond, which in this case bears a bromine substituent, at C-7, is characteristic of 7-norbornadienyl cations[1c].

The driving force of the rearrangement, which overcomes the allylic resonance in *(4)*, is most probably the lessening of strain energy on ring expansion *(4)*→*(8)* and the pronounced stability of *(9)*.

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German version: Angew. Chem. *88*, 508 (1976)

CAS Registry numbers:
(1), 59574-39-9; *(2)*, 50399-12-7; *(3)*, 52911-87-2; *(5)*, 59574-40-2; *(5)*-dinitrobenzoate, 59574-41-3; *(6)*, 59574-42-4; *(6)*-dinitrobenzoate, 59574-43-5; *(7)*, 59574-44-6; *(10)*, 59574-45-7; 3,5-dinitrobenzoyl chloride, 99-33-2; di-2,4,6-cycloheptatrienyl ether, 16273-47-5; AgBr, 7785-23-1; $AgClO_4$, 7783-93-9

[1] a) *G. A. Olah* and *P. v. R. Schleyer*: Carbonium Ions. Wiley-Interscience, New York; b) *R. E. Leone, J. C. Barborak*, and *P. v. R. Schleyer* in [1a], Vol. 4, p. 1837 (1973); c) *P. R. Story* and *B. C. Clark, Jr.* in [1a], Vol. 3, p. 1007 (1972).
[2] *M. Christl* and *G. Brüntrup*, Angew. Chem. *86*, 197 (1974); Angew. Chem. Int. Ed. Engl. *13*, 208 (1974).
[3] Elemental analyses and mass and ^{1}H-NMR spectra of all the new compounds accord with the given structures.
[4] *H. Prinzbach, H. Babsch*, and *H. Fritz*, Tetrahedron Lett. *1976*, 2129. We are indebted to Prof. *Prinzbach* for the agreement reached concerning the preparation of *(1)* from *(6)*.
[5] *B. Franzus, M. L. Scheinbaum, D. L. Waters*, and *H. B. Bowlin*, J. Am. Chem. Soc. *98*, 1241 (1976).
[6] In the absence of silver perchlorate, compound *(3)* is stable in this mixture.
[7] Cf. *E. I. Snyder* and *B. Franzus*, J. Am. Chem. Soc. *86*, 1166 (1964).

New Ring Transformation of Zwitterionic Bicyclic Thiazole Systems

By *Sang-Woo Park, Walter Ried*, and *Walter Schuckmann*[*]

Dedicated to Professor Dr. R. Wegler on the occasion of his 70th birthday

The reaction of phenacyl bromide *(2)* with the bicyclic zwitterionic thiazoles *(1a)* and *(1b)*, which result from a three-component reaction of cyclic thioureas, mercury bis-(phenylacetylide), and phenyl isothiocyanate[1,2], does not yield the bromides *(4)* corresponding to the iodides *(3)*[2]; instead ring opening and renewed cyclization affords the new bicyclic thiazoles 2-[2-(7-benzoyl-5-phenylimino-2,3-dihydro-1*H*-imidazo[1,2-*c*]thiazol-1-yl)-2-phenylvinylthio]acetophenone *(10a)* and 2-[2-(8-benzoyl-6-phenylimino-1,2,3,4-tetrahydrothiazolo[3,4-*a*]pyrimidin-1-yl)-2-phenylvinylthio]acetophenone *(10b)*, respectively.

Since no unequivocal structural information about products *(10)* could be derived from their spectroscopic data, the molecular structure of *(10a)* was solved by X-ray methods. The formula scheme shows the suspected mode of formation of these compounds. Simultaneous formation of the salt *(7)*[3,4] apparently results from a secondary reaction of the unstable primary product *(4)* under the action of *(1)*. Direct reaction of *(1)* with HBr likewise proceeds *via (5)* to give the salt *(7)*, from which the free base *(9)*[2] is obtained with aqueous K_2CO_3 solution. The phenyl isothiocyanate isolated by column chromatography can be trapped as *N,N'*-diphenylthiourea with aniline in methanol.

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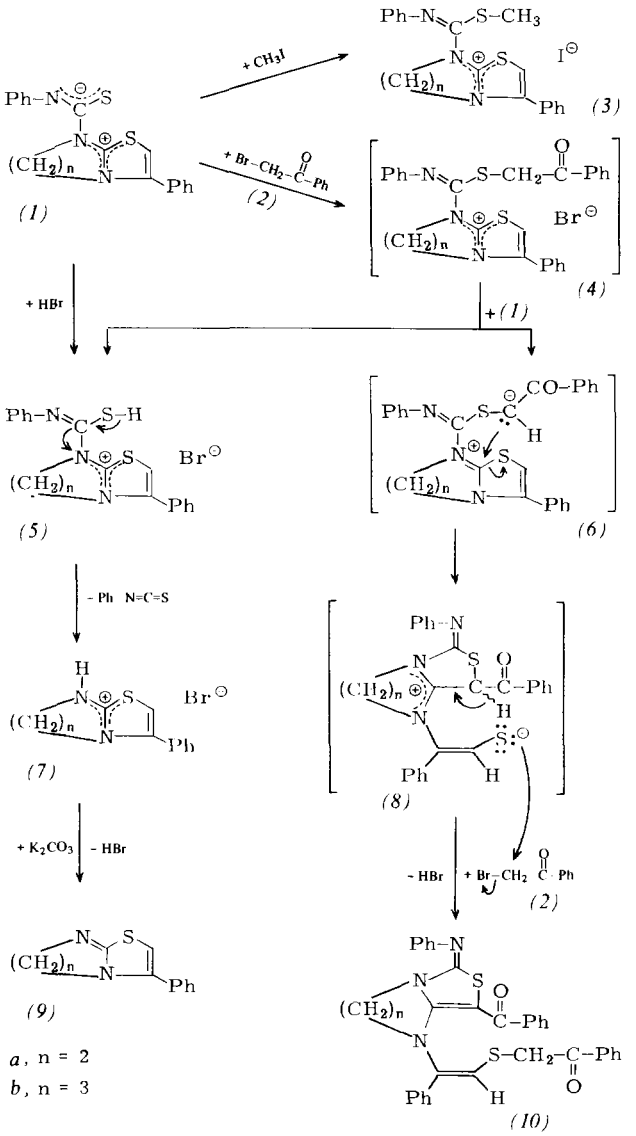

Table 1. Data for compounds *(10a)* and *(10b)* (correct elemental analyses and mass spectra are available).

	Yield [%]	M.p. [°C]	IR [a] [cm^{-1}]	^{1}H-NMR [b] [δ, ppm]
(10a)	40	197	3060 1680	3.86—4.2 (m; 6H) 6.06 (s; 1H) 6.68—7.96 (m; 20H)
(10b)	32	154	3060 1690	1.5—2.1 (m; 2H) 3.1—4.2 (m; 6H) 5.94 (s; 1H) 6.7—8.1 (m; 20H)

[a] ν(=CH) and ν(C=O) in KBr.
[b] Conditions: 100 MHz, $CDCl_3$, hexamethyldisiloxane as internal standard.

General procedure:

A solution of *(2)* (2 mmol) in acetone (10 ml) is added to a solution of *(1a)* in hot acetone (200 ml; 100 ml in the case of *(1b)*). After refluxing for 5 min and standing at room temperature for several hours the colorless crystals of *(7)* are filtered off and the solvent distilled from the filtrate in a rotary evaporator. After addition of a little chloroform and keeping at room temperature the residue is freed from insoluble components and once again evaporated to dryness. Column chromatography of the residue on silica gel (elution with benzene/ethyl acetate 3:1) furnishes *(10)*. Recrystallization from a little acetone in the cold gives yellow crystals.

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German version: Angew. Chem. 88, 511 (1976)

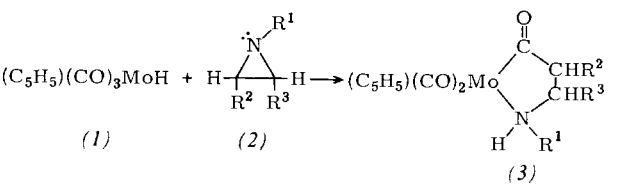
CAS Registry numbers:
(1a), 55139-32-7; *(1b)*, 55139-34-9; *(2)*, 70-11-1; *(10a)*, 59643-55-9; *(10b)*, 59643-56-0

[1] *W. Ried, R. Oxenius,* and *W. Merkel,* Angew. Chem. *84*, 535 (1972); Angew. Chem. Int. Ed. Engl. *11*, 511 (1972).
[2] *W. Ried, W. Merkel, S. W. Park,* and *M. Dräger,* Justus Liebigs Ann. Chem. *1975*, 79.
[3] *W. Wilson* and *R. Woodger,* J. Chem. Soc. *1955*, 2943; *M. Fefer* and *L. C. King,* J. Org. Chem. *26*, 828 (1961).
[4] *V. K. Chadha* and *H. K. Pujari,* Can. J. Chem. *47*, 2843 (1969).

Complete Asymmetric Synthesis and Absolute Configuration of an Aminoacylmolybdenum Complex

By *Wolfgang Beck, Wolfgang Danzer, Anh Thu Liu,* and *Gottfried Huttner*[*]

Previously described reactions of η^5-cyclopentadienyltricarbonyl hydrides of molybdenum *(1)* and tungsten with substituted aziridines *(2)*[1] suggested that the β-aminoacyl chelate complexes *(3)* are formed with asymmetric induction.



	R^1	R^2	R^3	*(2)*	*(3)* $[\alpha]_{578}^{23}$ [d]
a	Me	Ph	Me	$(-)_{578}$ [a]	−687°
b	Me	Ph	Me	$(+)_{578}$ [b]	+100°
c	H	H	Me		
d	H	Ph	H		
e	H	H	Et	$(+)_{578}$ [c]	+ 51.3°
f	*t*-Bu	H	H		

[a] *cis*-(2*R*,3*S*); [b] *trans*-(2*S*,3*S*); [c] (3*R*); [d] in acetone.

By reaction of *(1)* with the optically active aziridines *(2a)* and *(2b)* and X-ray structure analysis of the complex *(3a)* we found that complete asymmetric induction occurs at *two* prochiral centers in a specificity-determining step. IR spectra show that the aziridine *(2)* is initially protonated and then undergoes nucleophilic attack at C-2 by the carbonylmetalate ion. Ring opening is regiospecific; in *(2c)* the Mo atom is bonded to the unsubstituted C atom, and in *(2d)* to the phenyl-substituted one.

Reaction of *(2f)* affords the aminoalkyl complex *(4f)*. The intermediacy of the complexes *(4a)* to *(4e)* also follows from the fact that the compound *(5c)*[3], obtained according to *Knoth*[2], can be converted into the chelate complex *(3c)*.

Crucial steps for the stereospecific formation of *(3a)* from *(4a)* are the "CO insertion" and the coordination of the

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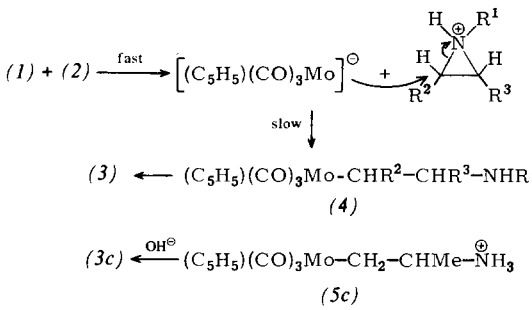
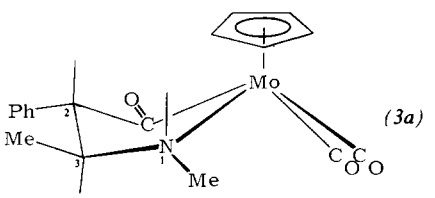
N atom to the metal. This fixes the asymmetric center at C-2; two new chiral centers are created at N and Mo. Of the 16 possible (considering the conformation of the chelate



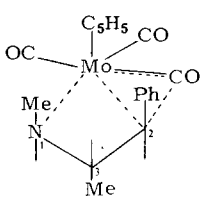
ring) diastereomeric complexes only the isomer *(3a)* is formed (Fig. 1), which does not epimerize in solution according to its ^{1}H- and ^{13}C-NMR spectra.



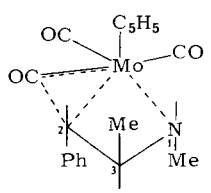
(3a)

Fig. 1. Structure of the tetragonal complex *(3a)* (schematic). S_{Mo}, 1*R*,2*S*,3*S*; space group $P4_12_12$; $a=b=1663\pm1$, $c=1449\pm1$ pm, $d_{X\text{-ray}}=1.26$, $d_{exp}=1.28\,g\,cm^{-3}$, $Z=8$, $R_1=5.6\,\%$ (measurements: Syntex P21; solution: Syntex XTL). Distances and angles expectedly resemble those in the analogous compound *(3)*, $R^1=R^2=R^3=H$ [4]. The absolute configuration depicted follows from the finding that the configuration at the methyl-substituted C atom of the aziridine *(2a)* is retained [5].

The established reaction mechanism requires that the aziridine *(2a)* is opened with inversion at C-2 (*R*→*S*). In contrast, the migration of the alkyl group to the carbonyl carbon atom proceeds with retention[6]. The orientation of the aminoalkyl group in the diastereomeric transition states R_{Mo}-*(6a)* and S_{Mo}-*(6a)* determines the asymmetry at the molybdenum atom. (R_{Mo} and S_{Mo} are defined by viewing the tetragonal pyramid in Fig. 1 from above). CO insertion and N coordination do not necessarily proceed synchronously.



R_{Mo}-*(6a)*



S_{Mo}-*(6a)*

We assume that the transition state R_{Mo}-*(6a)* is energetically less favorable than S_{Mo}-*(6a)* owing to nonbonding intramolecular interactions between the "upward" pointing methyl and phenyl groups and the π-bonded cyclopentadienyl ring. For the chiral chelate ring the δ-conformation is found; only in this conformation are the three ring substituents in the energetically favorable equatorial position.

Applying the same considerations to the reaction of *(1)* with *(2e)* would indicate the resulting complex *(3e)* also to have the S_{Mo} configuration. In fact the CD spectra of *(3a)* and *(3e)* are practically identical, while the CD spectra of *(3a)* and *(3b)* are related as object and mirror image in the range 200—380 nm. Hence the expected R_{Mo} configuration can be deduced for *(3b)*.

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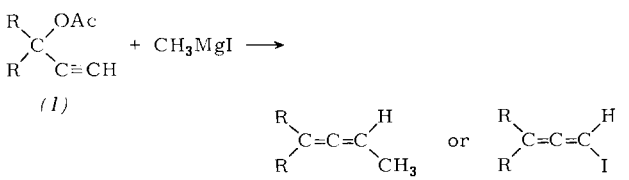
CAS Registry numbers:
(1), 12176-06-6; *(2a)*, 2242-90-2; *(2b)*, 13148-28-2; *(2e)*, 6189-23-7; *(3a)*, 59727-68-3; *(3b)*, 59672-01-4; *(3e)*, 59672-00-2

[1] *W. Beck*, *W. Danzer*, and *R. Höfer*, Angew. Chem. *85*, 87 (1973); Angew. Chem. Int. Ed. Engl. *12*, 77 (1973).
[2] *W. H. Knoth*, Inorg. Chem. *7*, 1566 (1975).
[3] *B. Olgemöller*, Diplomarbeit, Universität München 1976.
[4] *G. A. Jones* and *L. J. Guggenberger*, Acta Crystallogr. *B31*, 900 (1975).
[5] The absolute configuration of an analogous optically active tetragonal-pyramidal molybdenum complex was described by *S. J. La Placa*, *I. Bernal*, *H. Brunner*, and *W. A. Hermann* (Angew. Chem. *87*, 379 (1975); Angew. Chem. Int. Ed. Engl. *14*, 353 (1975)).
[6] Cf. *G. M. Whitesides* and *D. J. Boschetto*, J. Am. Chem. Soc. *91*, 4131 (1969); *H. Brunner*, Top. Curr. Chem. *56*, 67 (1975).

Trialkylallenes from 1,1-Disubstituted Propargylic Acetates

By *Françoise Delbecq* and *Jacques Gore*[*]

We recently reported that the reaction of 1.2 molar equivalents of methylmagnesium iodide with 1,1-disubstituted propargylic acetates *(1)* in ether leads selectively to methylallenes or iodoallenes depending on the experimental conditions[1].



We now report that this reaction can be extended to other Grignard reagents, providing a convenient entry to trialkylallenes *(2)*. The best conditions for obtaining the trialkylallenes consist in adding the solution of the Grignard reagent in ether to a solution of 1 mol of acetate *(1)* and 4 mols of magnesium bromide in the same solvent. All the reactions listed in Table 1 were performed in this way. The number of molar equivalents of the Grignard reagent depends on the type of halide and the ease of formation and further reaction of the radical R·.

The reaction is less satisfactory with Grignard reagents of secondary halides; iodides give better results than bromides but in spite of numerous attempts it was impossible to find conditions under which very good yields of allenes and extensive conversion of acetate could be both maintained. With larger quantities of reagent or increased reaction times, the yields are lower and the reaction product is mainly composed of high molecular unidentified compounds.

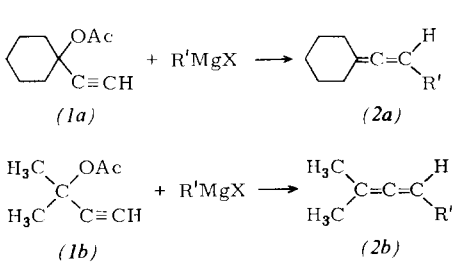


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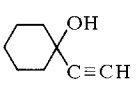
Table 1. Reaction of acetates *(1a)* or *(1b)* (in each case 2g; exception: Nos. 1 and 2, each 10g) with 2mol Grignard reagent (exception: Nos. 5 to 8, each 4mol Grignard reagent) to give allenes of type *(2a)* and *(2b)*, respectively. Their IR, NMR, and mass spectra resemble these of *(2aa)*.

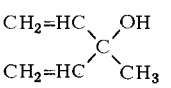
No. *(1)*	Grignard reagent from	Allene	R′ in *(2a)* or *(2b)*	Yield [%]	Residual *(1)* [%]
1 *(1a)*	1-Iodopropane	*(2aa)*	n-C_3H_7	72 [a]	0
2 *(1b)*	1-Iodooctane	*(2bb)*	n-C_8H_{17}	64 [b]	0
3 *(1a)*	5-Iodo-1-pentene	*(2ac)*	$(CH_2)_3$—CH=CH_2	60 [b]	0
4 *(1a)*	2-Iodopropane	*(2ad)*	i-C_3H_7	44 [b]	28
5 *(1a)*	2-Iodobutane	*(2ae)*	*sec*-C_4H_9	68 [b]	0
6 *(1b)*	2-Iodooctane	*(2bf)*	$CH(CH_3)$—C_6H_{13}	20 [b]	25
7 *(1a)*	2-Bromo-2-methylpropane	*(2ag)*	*tert*-C_4H_9	80 [a]	0
8 *(1a)*	2-Bromo-2-methylbutane	*(2ah)*	$C(CH_3)_2$—C_2H_5	55 [b]	0
9 *(1a)*	Iodobenzene	*(2ai)*	C_6H_5	10	

[a] Purification by column chromatography on silica gel (eluant: petroleum ether).
[b] Isolation by preparative thin-layer chromatography.

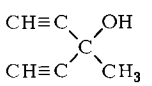
The same reaction was attempted with *(1a)* using unsaturated Grignard reagents. Phenylmagnesium iodide gives only 10% of the corresponding allene β-cyclohexylidenestyrene *(2ai)* besides 1-ethynylcyclohexanol *(3)*. Grignard reagents from allyl and propargyl bromides lead exclusively to a mixture of alcohols *(3)*, *(4)* and *(5)*.



(3)



(4)



(5)

1-Cyclohexylidene-1-pentane (2aa)

(1a) (10g, 0.06mol) is added to the solution of $MgBr_2$ (0.24mol) (from 45g of 1,2-dibromoethane and 5.85g of Mg) in ether (110ml) and the solution so obtained is stirred for 30min at 25°C. The solution of Grignard reagent prepared by the usual method from 20.5g (0.12mol) of *n*-propyl iodide, 2.93g (0.12mol) of magnesium in 100ml of ether is then added under N_2 at such a rate that reflux is maintained. On completion of the addition, stirring is continued for a further 30min. The bottom layer is separated and extracted with ether (3×50ml). The combined extracts are added to the upper layer which is slowly hydrolyzed with about 50ml of 5% aqueous NaOH. Usual workup and chromatography over silica gel (Merck 70-230 mesh) with petroleum ether give 6.5g (72%) of gas- and thin-layer-chromatographically pure *(2aa)*. IR: ν(C=C=C)=1965 cm^{-1}; MS: *m/e* 150 (17%) $M^{\bullet+}$; 79 (100%); ^{1}H-NMR: $\delta(CCl_4)$=0.92 (t, 3H, J=6.5 Hz); 1.15—1.90 (10H); 1.90—2.30 (4H); 4.88 (1H, t×quintuplet, J=6 and 2 Hz).

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German version: Angew. Chem. 88, 537 (1976)

CAS Registry numbers:
(1a), 5240-32-4; *(1b)*, 1604-29-1; 1-pentene *(2aa)*, 59643-57-1; *(2ac)*, 59643-58-2; *(2ad)*, 59643-59-3; *(2ae)*, 59643-60-6; *(2ag)*, 59643-61-7; *(2ah)*, 59643-62-8; *(2ai)*, 59643-63-9; *(2bb)*, 56956-49-1; *(2bf)*, 59643-64-0; 1-iodopropane, 107-08-4; 1-iodooctane, 629-27-6; 5-iodo-1-pentene, 7766-48-5; 2-iodopropane, 75-30-9; 2-iodobutane, 513-48-4; 2-iodooctane, 557-36-8; 2-bromo-2-methylpropane, 507-19-7; 2-bromo-2-methylbutane, 507-36-8; iodobenzene, 591-50-4

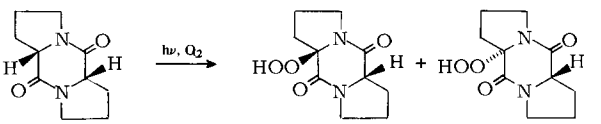
[1] *M. L. Roumestant* and *J. Gore*, Bull. Soc. Chim. Fr. *1972*, 591; *F. Coulomb-Delbecq* and *J. Gore*, J. Organometal. Chem. *87*, C23 (1975); *F. Coulomb-Delbecq*, *M. L. Roumestant*, and *J. Gore*, Bull. Soc. Chim. Fr. *1976*, 533; *F. Coulomb-Delbecq* and *J. Gore*, *ibid. 1976*, 541.

Radical Oxidation of Amino Acid Derivatives

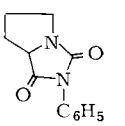
By *Ulrich Schmidt* and *Johannes Häusler*[*]

Dedicated to Professor Helmut Zahn

In recent years, derivatives—and especially dioxopiperazines—of α-hydroxy, α-mercapto, and α,β-dehydro amino acids have frequently been discovered as fungal metabolites[1]. Consideration of their biosynthesis prompted us to investigate the autoxidation of dioxopiperazines such as *(1)*: we found that they undergo ready oxidation to hydroperoxides such as *(2)* and *(3)*. The latter can easily be reduced to alcohols which are transformed into mercaptodioxopiperazines by hydrogen sulfide[2].



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



(4)

Dioxopiperazines are cyclic dipeptides. Their autoxidation can be performed photochemically with benzophenone as sensitizer, or in the dark by the action of radical initiators (peroxides, azo compounds) under oxygen pressure. In some cases the reaction with illumination occurs particularly readily and it is difficult to understand how this sensitivity of cyclic dipeptides has hitherto escaped notice: a 3,6-diethyl-1,4-dimethyl-2,5-piperazinedione preparation stored for four years in a poorly sealed bottle was found to have undergone almost complete oxidation to a mixture of mono- and bis-hydroperoxide. Practically all dioxopiperazine derivatives stored without exclusion of oxygen are found to contain peroxide after a certain time.

cyclo(-L-Pro-L-Pro) *(1)*, *cyclo*(-L-Pro-Gly-), *cyclo*(-L-Pro-Sar-), and 3,6-diethyl-1,4-dimethyl-2,5-piperazinedione were oxidized to mono- and bis-hydroperoxides. The *N*-phenylhydantoin derivative *(4)* could only be oxidized to the monohydroperoxide with the aid of peroxidic catalysis.

The reaction conditions will be presented for compound *(1)* as an example. 15 hours' irradiation (Rayonet reactor, 350-nm light) of *(1)* in ethyl acetate with 1 mol% of benzophenone under an oxygen pressure of 5 atm leads to almost complete conversion into a mixture, of which approximately one half was composed of *cis*-monohydroperoxide *(2)* and *cis*-bishydroperoxide. The major product is *(2)* if oxidation is performed for a shorter period. The best yields of *(2)* are obtained on reaction in daylight (see *Procedure*).

cis- and trans-cyclo(-α-Hydroperoxy-L-Pro-L-Pro-), (2) and (3) respectively

A solution of *(1)* (1.98g) and benzophenone (20mg) in distilled ethyl acetate (50ml) was exposed to sunlight (Vienna, July, largely unclouded) in a 100-ml Erlenmeyer flask. Deposition of hydroperoxides in the form of bundle-like crystals began within two days. The crystalline reaction product was

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filtered off every two days (crude yield 90 %). Recrystallization from chloroform/ethyl acetate removes precipitated *(1)*. Separation of *(2)* and *(3)* (ratio 94:6) and traces of *trans*-bis-hydroperoxide was accomplished by column chromatography (Kieselgel 60, Merck; ethyl acetate/ethanol 4:1). *(2)* and *(3)* form colorless crystals of dec. pt. >140°C (racemic *(2)*, cf. ref. [2a]).

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German version: Angew. Chem. *88*, 538 (1976)

CAS Registry numbers:
(1), 19943-27-2; *(2)*, 59685-08-4; *(3)*, 59643-65-1

[1] *H. Poisel* and *U. Schmidt*, Chem. Ber. *108*, 2547 (1975), and references cited therein; *P. G. Sammes*, Fortschr. Chem. Org. Naturst. *32*, 51 (1975).
[2] a) *E. Öhler*, *F. Tataruch*, and *U. Schmidt*, Chem. Ber. *106*, 165 (1973); b) *ibid. 106*, 396 (1973); c) *J. Häusler* and *U. Schmidt*, *ibid. 107*, 2804 (1974).

Self-Condensation of β-Dialkylaminocrotonates: A One-Step Synthesis of *N,N*-Dialkylanthranilates[**]

By *Roger L. N. Harris*, *John L. Huppatz*, and *John N. Phillips*[*]

The self-condensation of ethyl β-aminocrotonate in the presence of phosphorus oxide chloride to give the pyridine *(3)* was first reported in 1901[1]. A key step in this reaction is the utilization of the nitrogen atom from one amino group in the formation of the heterocyclic ring. We now report that in the analogous reaction of *N,N*-dialkylaminocrotonates *(1)*, where heterocyclic ring formation is not possible without dealkylation, self-condensation follows a different path, leading in high yield to *N,N*-dialkylanthranilic acid derivatives.

When ethyl β-dimethylaminocrotonate *(1a)* was allowed to react with an excess of $POCl_3$, a mildly exothermic reaction ensued. On work-up, a pale yellow oil was obtained, for which analytical and high resolution mass spectral data indicated the formula $C_{12}H_{16}ClNO_2$. The compound had arisen, therefore, by self-condensation of the crotonate *(1a)*, elimination of dimethylamine, water and ethanol, and addition of HCl. The NMR spectrum ($CDCl_3$) was consistent with a benzene structure bearing ethoxycarbonyl, methyl, chloro and dimethylamino substituents. The remaining two aromatic protons appeared as two broad singlets at $\delta = 6.70$ and 6.75.

The chloro substituent was removed by catalytic hydrogenolysis and the resulting ester hydrolyzed to give 4,*N*,*N*-trimethylanthranilic acid, identical with an authentic sample prepared by reaction of 2-chloro-4-methylbenzoic acid[2] with dimethylamine in DMF in the presence of copper acetate. Chlorination of the original self-condensation product with sulfuryl chloride in chloroform at room temperature gave a fully substituted trichlorobenzene derivative, indicating that the two unsubstituted positions originally present must have been *ortho* and *para* to the dimethylamino group. The self-condensation product is therefore ethyl 6-chloro-4,*N*,*N*-trimethylanthranilate *(2a)*.

The reaction appears to be generally applicable to *N,N*-dialkyl-β-aminocrotonates (see Table 1).

Ethyl 6-chloro-4,N,N-trimethylanthranilate (2a)

(1a) (100 g) was added slowly with stirring to $POCl_3$ (500 ml) cooled externally by a bath of tap-water. The addition was controlled so that the temperature did not exceed 35°C. The mixture was kept overnight then heated on a steambath for

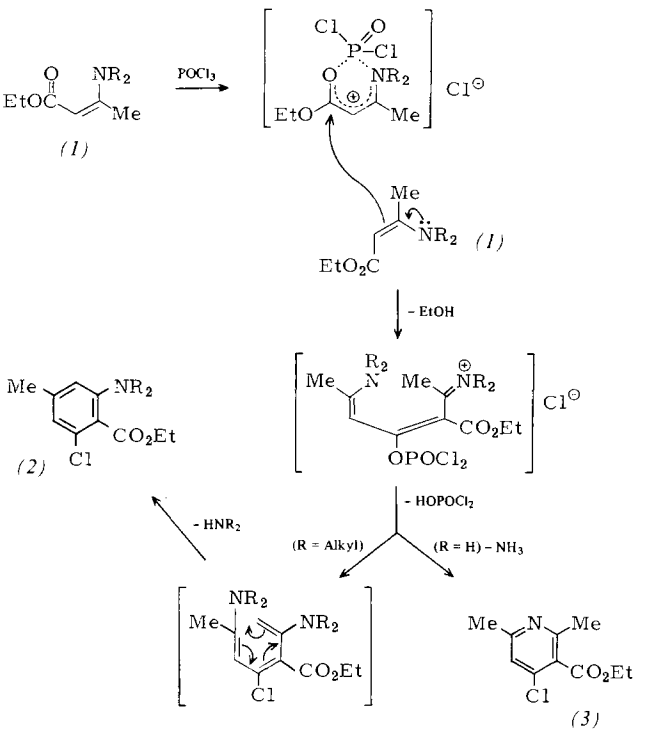

Table 1. Ethyl *N,N*-dialkylanthranilates *(2)* prepared from ethyl β-dialkylaminocrotonates *(1)*.

	R	R	Yield [%]	B.p. [°C/torr]
a	CH_3	CH_3	78	124—128/1.0
b	C_2H_5	C_2H_5	88	130—132/1.0
c		$-(CH_2)_4-$	89	[a]
d		$-(CH_2)_5-$	89	160—163/1.0

[a] M.p. 78—79°C; prisms from methanol.

1 h. Excess $POCl_3$ was removed *in vacuo* (rotary evaporator) and the residual brown oil treated with 2 liters of icewater. After hydrolysis of residual $POCl_3$ was complete the product was extracted with chloroform (3 × 150 ml), the combined extracts dried by filtration over $MgSO_4$ and the chloroform removed *in vacuo*. The residual oil (80 g) was distilled *in vacuo* to give *(2a)* as a pale yellow oil; yield 60 g (78 %), b.p. 124—128°C/1.0 torr.

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CAS Registry numbers:
(1a), 14205-42-6; *(1b)*, 59222-31-0; *(1c)*, 2723-42-4; *(1d)*, 36276-69-4; *(2a)*, 59686-37-2; *(2b)*, 59686-38-3; *(2c)*, 59686-39-4; *(2d)*, 59686-40-7; $POCl_3$, 10025-87-3

[1] *A. Michaelis* and *K. von Arend*, Ber. Dtsch. Chem. Ges. *34*, 2284 (1901).
[2] *A. A. Goldberg* and *A. H. Wragg*, J. Chem. Soc. *1958*, 4227.

Fluoride Catalyzed Addition of Silylacetylenes to Carbonyl Compounds

By *Eiichi Nakamura* and *Isao Kuwajima*[*]

Recent developments in the methodology of generating quaternary ammonium enolates[1] have revealed unparalleled reactivities of such species[2]. Moreover, methods for the synthesis of enols without resort to the use of either strongly

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[**] Amide—Acid Chloride Adducts in Organic Synthesis. Part 7.—Part 6: Aust. J. Chem., in press.

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acidic or basic reagents have been developed[1]. We report here on the reactivities of previously unknown acetylides *(2)* generated from trimethylsilylacetylenes such as *(1)* and carbonyl compounds *(3)*. Synthetic reactions in strongly acidic solution, in which an acetylene is activated by a silyl group have been described[3]. The method reported here is the first example of such a use of silyl groups under essentially neutral conditions.

A catalytic amount of tetrabutylammonium fluoride[2] effects the addition of 1-phenyl-2-trimethylsilylacetylene *(1)* to carbonyl compounds *(3)*, *e.g.* aldehydes, and aliphatic and aromatic ketones. The reaction, usually conducted in THF with about 3 mol % of the catalyst, proceeds smoothly at temperatures ranging from −78° to +25°C, and the product yield is generally good (Table 1). Adducts can be isolated either in the silylated form *(4)* or, after hydrolysis with dilute acetic acid, as alcohols *(5)*. α,β-Unsaturated ketones, however, behave in a rather complicated way. While chalcone *(3f)* affords exclusively the adduct *(4f)* in good yield, common conjugated ketones, *e.g.* 2-cyclohexenone, methyl vinyl ketone, benzylidine acetone gave only little or no adducts of type *(4)*. Thus the acetylide *(2)* is less reactive than the corresponding lithium phenylacetylide which afforded satisfactory results also with conjugated ketones. The catalyzed reaction most likely proceeds as shown in the following Scheme[1].

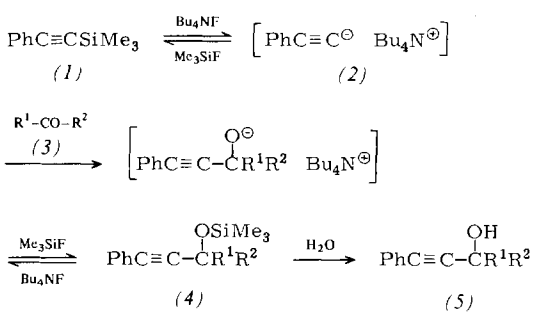

Table 1. Tetrabutylammonium fluoride catalyzed reaction of 1-phenyl-2-trimethylsilylacetylene *(1)* with carbonyl compounds *(3)*. The reaction was carried out in THF at −20°—0°C with 3 mol % of catalyst.

	R^1	R^2	*(4)* Yield [%]	*(5)* Yield [%]
a	H	Ph	76	
b	H	*n*-C_7H_{15}	70	
c	H	*i*-Bu		84
d	H	$CH{=}CMe(CH_2)_2CH{=}CMe_2$ [a]	62	
e	Ph	Ph	79	
f	Ph	CH=CH—Ph	83	
g	Ph	Et		72
h		$-(CH_2)_5-$	87	

[a] Citral.

The method can also be applied to silylacetylenes other than *(1)*. For instance, 1-trimethylsilyl-1-octyne reacts at room temperature with benzophenone to furnish the adduct in good yield.

Recently, a general route to 1-aryl-2-trialkylsilylacetylenes[4] as well as a procedure for the silylation of acetylenes under neutral conditions[2] have been reported. The extremely mild conditions combined with the accessibility of the silylacetylenes will render this catalyzed reaction a valuable synthetic aid.

1-(Phenylethynyl)-1-trimethylsiloxycyclohexane (4h)

A solution of *(1)* (287 mg, 1.65 mmol) and *(3h)* (147 mg, 1.50 mmol) in THF (2 ml) was treated with tetrabutylammonium fluoride (14 mg, 0.05 mmol) at −20°C for 5 min, and then at 0°C for 1 h. The yellow reaction mixture was diluted with hexane, and filtered. After concentration, the residual yellow oil was purified by preparative thin-layer chromatography; yield 354 mg (87 %), b.p. 115°—117°C/1.0 torr.

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German version: Angew. Chem. *88*, 539 (1976)

CAS Registry numbers:
(1), 2170-06-1; *(3a)*, 100-52-7; *(3b)*, 124-13-0; *(3c)*, 590-86-3; *(3d)*, 5392-40-5; *(3e)*, 119-61-9; *(3f)*, 94-41-7; *(3g)*, 93-55-0; *(3h)*, 108-94-1; *(4a)*, 59738-52-2; *(4b)*, 59738-53-3; *(4d)*, 59738-54-4; *(4e)*, 59738-55-5; *(4f)*, 59738-56-6; *(4h)*, 59738-57-7; *(5c)*, 15212-29-0; *(5g)*, 59738-58-8; Bu_4NF, 429-41-4

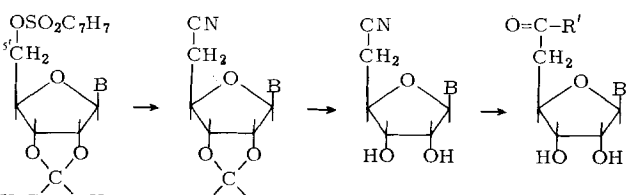
[1] *I. Kuwajima* and *E. Nakamura*, J. Am. Chem. Soc. *97*, 3257 (1975); *E. Nakamura, M. Shimizu*, and *I. Kuwajima*, Tetrahedron Lett., in press.
[2] *E. Nakamura, T. Murofushi, M. Shimizu*, and *I. Kuwajima*, J. Am. Chem. Soc. *98*, 2346 (1976).
[3] *L. Birkofer, A. Ritter*, and *H. Uhlenbrauck*, Chem. Ber. *96*, 3280 (1963); *D. R. M. Walton* and *F. Waugh*, J. Organomet. Chem. *37*, 45 (1972); *P. Burgeois, G. Merault*, and *R. Calas*, *ibid.* *59*, C4 (1973).
[4] *R. Oliver* and *D. R. M. Walton*, Tetrahedron Lett. *1972*, 5209.

Facile Preparation of 5′-Cyano- and 5′-Carboxynucleosides[**]

By *Wilfried Meyer, Ekkehard Böhnke*, and *Hartmut Follmann*[*]

Nucleoside derivatives substituted at the exocyclic C5′-atom of the ribose moiety are important for the elucidation of structure-function relations in naturally occurring nucleosides and nucleotides and as potential drugs[1–4]. While substitution at C5′ by O, N, S, and halogen functions is generally easy[4, 5], a C—C chain elongation at this site to give "homonucleosides" is possible in only few cases and generally in unsatisfactory yield[1, 2, 6].

We have now found a facile synthesis of 5′-deoxy-5′-cyanonucleosides *(2)* and *(3)* and the 5′-deoxynucleoside-5′-carboxylic acids *(5)* derived from these nitriles. Reaction of the readily accessible 2′,3′-*O*-isopropylidene-5′-*O*-tosyl derivatives of nucleosides such as *(1a)* in dioxane or acetonitrile with alkali cyanides with addition of equimolar amounts of the complexing agent [18]crown-6[7] smoothly affords, *e.g.*, *(2a)*; basic elimination of the aglycon[8], which readily occurs under similar conditions, is not observed; nor is intramolecular cyclization of *(1a)* to give N^3,5′-cycloadenosine. Compound *(1b)* yields not only *(2b)* but also the readily separable O^2,5′-cyclouridine. Compounds *(1a)* and *(1b)* failed to react with cyanides under all tested variations of temperature and solvent when the reaction was attempted without crown ether catalysis. The more reactive 5′-deoxy-5′-iodonucleosides



(1a), (1b) *(2a), (2b)* *(3a), (3b)* *(4a)*, R′ = NH_2 *(5a)*, R′ = OH

a, B = Adenine; *b*, B = Uracil

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give only small amounts of the 5'-cyanides beside cyclization and degradation products, regardless of whether a crown ether is present or not[9].

The new compounds, whose structures are confirmed by mass spectra, UV spectra [*(2a)*: $\lambda_{max}=259$ nm; *(2b)*: 258 nm in H_2O, pH 7], and a characteristic IR absorption band at 2250 cm^{-1}, can be divested of the ketalic 2',3' protective function by acid treatment. The water-soluble 5'-deoxy-5'-cyanonucleosides *(3a)* and *(3b)* provide an entry to the nucleosides of 5'-deoxy-β-D-*ribo*hexafuranuronic acid which were formerly inaccessible by a simple pathway. Thus hydrolysis of *(3a)* in alkaline hydrogen peroxide gave both the amide *(4a)* and the 5'-deoxyadenosine-5'-carboxylic acid *(5a)*. Hitherto only analogous carboxylic acid derivatives stemming from adenosine itself were known which are formed as C5'-OH epimer mixtures (cf. ref. [2]). *(5a)* closes the gap between adenosine-5'-uronic acid and 5'-deoxyadenosine-5'-acetic acid[1] and like the latter carboxylic acid is also a model compound for adenosine-5'-phosphate (AMP); for instance, *(5a)* is deaminated to the inosine derivative by the enzyme AMP aminohydrolase (EC 3.5.4.6).

Like the natural nucleosides, *(3a)*, *(3b)*, and *(5a)* in aqueous solution prefer the *anti* conformation of the base relative to the C—N glycosidic bond. This is deduced from the typical downfield shift of the ring proton signals in the ^{1}H-NMR spectrum by the adjacent polar 5'-substituent[10]. *(5a)* exhibits the same long-wave CD spectrum as AMP ($[\Theta]_{260}=-4800$ deg cm^2 $dmol^{-1}$). However, the CD spectrum of *(3a)* displays an exceptionally low ellipticity and in the short-wave region a high ellipticity ($[\Theta]_{260}=-1300$, $[\Theta]_{210}=+7000$ deg cm^2 $dmol^{-1}$); this behavior confirms the relation deduced between structure, conformation, and circular dichroism for other adenosine derivatives with strongly polar 5'-substituents[10].

5'-Deoxy-5'-cyanoadenosine (3a)

Compound *(1a)* (0.92 g, 2 mmol) and [18]crown-6 (0.20 g) are stirred vigorously in anhydrous dioxane (15 ml) with dried KCN (0.65 g, 10 mmol) at room temperature for 20 h. Removal of the solid salts and preparative layer chromatography of the concentrated solution on silica gel with chloroform/methanol (6:1) ($R_f=0.74$) afford *(2a)* (0.35 g, 55 %) which crystallizes as needles (m. p. 202—204 °C) from methanol.—In order to remove the protecting group, *(2a)* (0.32 g) is suspended in 50 % formic acid (5 ml) and left to stand for 5 d at room temperature. Concentration *in vacuo* and freeze drying of the residue from water give a quantitative yield (0.27 g) of pure *(3a)*.

5'-Deoxyadenosine-5'-carboxamide (4a) and -5'-carboxylic acid (5a)

Compound *(3a)* (0.27 g, 1 mmol) is warmed to 30 °C for 1 h in 5% H_2O_2 (5 ml) (pH 10). The solution is then applied to an anion exchange column (formate form) and eluted with a water/formic acid gradient (pH 5 to pH 2) to give the amide *(4a)* (0.16 g, 55 %), a little adenine, and the carboxylic acid *(5a)* (0.07 g, 26 %). Direct hydrolysis of *(4a)* in more strongly alkaline solution led mainly to elimination of adenine.

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CAS Registry numbers:
(1a), 5605-63-0; *(1b)*, 7354-93-0; *(2a)*, 59696-80-9; *(2b)*, 59696-81-0; *(3a)*, 59696-82-1; *(3b)*, 59696-83-2; *(4a)*, 59696-84-3; *(5a)*, 59696-85-4

[1] *H. Follmann*, Angew. Chem. *86*, 41 (1974); Angew. Chem. Int. Ed. Engl. *13*, 77 (1974); *T. E. Walker, H. Follmann*, and *H. P. C. Hogenkamp*, Carbohyd. Res. *27*, 225 (1973).

[2] *P. Howgate* and *A. Hampton*, Carbohyd. Res. *21*, 309 (1972); *A. Hampton, P. Howgate, P. J. Harper, F. Perini, F. Kappler*, and *R. K. Preston*, Biochemistry *12*, 3328 (1973); *A. Hampton* and *R. R. Chawla*, J. Carbohyd., Nucleosid. Nucleotid. *2*, 281 (1975).

[3] *J. J. Baker, A. M. Mian*, and *J. R. Tittensor*, Tetrahedron *30*, 2939 (1974); *J. J. Baker, P. Mellish, C. Riddle, A. R. Somerville*, and *J. R. Tittensor*, J. Med. Chem. *17*, 764 (1974).

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[6] *J. A. Montgomery, A. G. Laseter*, and *K. Hewson*, J. Heterocycl. Chem. *11*, 211 (1974).

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[8] *H. Follmann*, Tetrahedron Lett. *1973*, 397.

[9] This reaction has formerly only been accomplished with thymidine: *G. Etzold, G. Kollowik*, and *P. Langen*, Chem. Commun. *1968*, 422.

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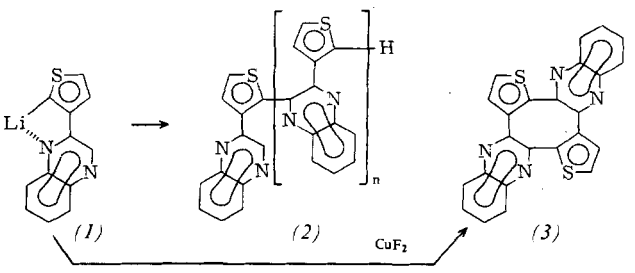
CuF_2-Assisted Synthesis of Heterocyclotetraaromatics by Nucleophilic Aromatic Substitution[**]

By *Thomas Kauffmann* and *Rolf Otter*[*]

Ten heterocyclopolyaromatics[1] were recently prepared in low yield (<26 %)[2] as the first representatives of a new class of substances.

The apparently obvious idea of cyclizing a monolithiated diheteroaromatic like *(1)* containing a strongly nucleophilic and a strongly electrophilic center by double nucleophilic aromatic substitution has not yet been realized. Thus the lithium compound *(1)*, obtained almost quantitatively from the metal-free compound by the action of lithium diisopropylamide, does not yield *(3)* on warming to 34 °C in ether[3] but instead gives the open-chain oligomers *(2)* ($n=1$—5, m. p. 170, 183, 196—198, 227, 242—244 °C, yields 10, 12, 13, 9, 5 %)[4]. This could be a consequence of the chelate bridge in *(1)* which fixes the two reactive centers in the *trans* position unfavorable for cyclization.—The desired cyclization to give *(3)* (m.p. 372—374 °C; yield 9 %) only occurred on treatment of the solution of *(1)* in THF at −20 °C with anhydrous CuF_2 in the molar ratio 1:2.



Unlike *(1)*, the benzo-homologs *(4)* also cyclize without addition of CuF_2. Addition of anhydrous CuF_2 or NiF_2 in the molar ratio 1:2 did however enhance the yield of *(6)* (m. p. 419—420 °C) from 11 to 63 (experiment 3 in Table 1). Thus a heterocyclopolyaromatic has now become available for the first time in preparatively useful yield.—Comparison of the experiments 1, 2, and 4 in Table 1 reveals that CuF_2 also promotes formation of the open-chain dimer *(5)*, $n=1$ (m. p. 231 °C) and the open-chain trimer *(5)*, $n=2$ (m. p. 348—349 °C).

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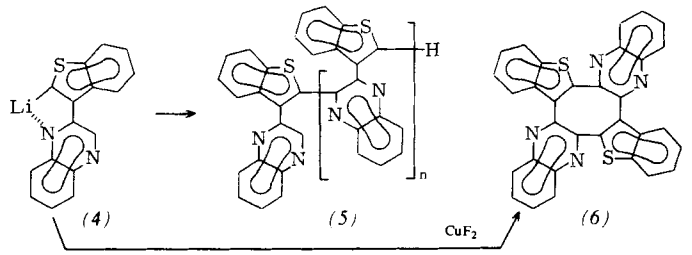
[**] Heterocyclopolyaromatics, Pat. 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. Refs. [2a—2c] are to be regarded as Parts 1 to 3.



Preliminary model studies[5] showed that CuF_2 and NiF_2 also favor formation of 2-(2-thienyl)pyridine from 2-lithiothiophene and 2-fluoropyridine: under the reaction conditions employed [30 min −40 °C, 4 h 0 °C, 30 min 20 °C in ether/THF (*ca.* 1 : 1)] the thienylpyridine was formed in 8 % yield without addition of metal fluoride, and in 24 and 12 % yield respectively on addition of NiF_2 and CuF_2 in the molar ratio 1 : 2.—The mode of action of the two transition metal fluorides is still a matter of conjecture.

Table 1. Effect of CuF_2 on the cyclization of *(4)* in THF [3, 4].

Run	*(4)*: CuF_2	Reaction temp. [°C]	Reaction time [h]	Recovery or yield [%] *(5)* $n=0$	*(5)* $n=1$	*(5)* $n=2$	*(6)*
1	1 : 0	−55	1/2	50	—	1	11
		+30	5				
2	1 : 2.0	−30	1/2	14	—	23	18
		+20	5				
3	1 : 2.0	−55	1/2	11	—	—	63
		−20	20				
4	1 : 1.0	−55	1/2	38	17	13	21
		−20	20				
5	1 : 0.5	−55	1/2	61	4.5	1	12
		−20	20				

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CAS Registry numbers:
(1), 59710-54-2; *(2)*, $n=1$, 59696-70-7; *(2)*, $n=2$, 59696-71-8; *(2)*, $n=3$, 59696-72-9; *(2)*, $n=4$, 59696-73-0; *(2)*, $n=5$, 59696-74-1; *(3)*, 59696-75-2; *(4)*, 59710-53-1; *(5)*, $n=0$, 59696-76-3; *(5)*, $n=1$, 59696-77-4; *(5)*, $n=2$, 59696-78-5; *(6)*, 59696-79-6; CuF_2, 7789-19-7

[1] The term "heterocyclopolyaromatics" includes compounds which, like 4,6,4‴,6‴-tetraaza-*m*-hexaphenylene [2c], contain not only heterocyclic units but also carbocyclic nuclei as ring members, and is therefore more convenient than "cyclopolyheteroaromatics" as a collective designation.

[2] a) *B. Greving, A. Woltermann*, and *Th. Kauffmann*, Angew. Chem. *86*, 475 (1974); Angew. Chem. Int. Ed. Engl. *13*, 467 (1974); b) *Th. Kauffmann, B. Greving, J. König, A. Mitschker*, and *A. Woltermann, ibid. 87*, 745 (1975) and *14*, 713 (1975) respectively; c) *Th. Kauffmann, B. Muke, R. Otter*, and *D. Tigler, ibid. 87*, 746 (1975) and *14*, 714 (1975), respectively.

[3] All solvents listed contained *ca.* 10 % of *n*-hexane introduced with *n*-butyllithium.

[4] Since the elimination step of the substitution reaction is only incomplete, if it occurs at all, rearomatization required oxidation with $KMnO_4$ in acetone after hydrolysis.

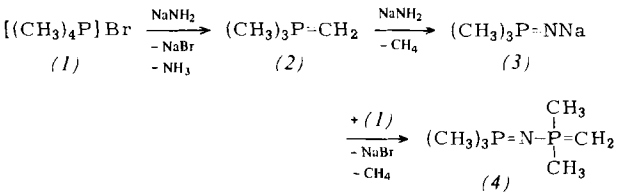
[5] Experiments by *H. Lexy*, Dissertation, Universität Münster, planned for 1977. Other experiments by *R. Otter*, Dissertation, Universität Münster, planned for 1976.

A Methylene-di-λ^5-phosphazene by Amide Cleavage of Tetramethylphosphonium Salts

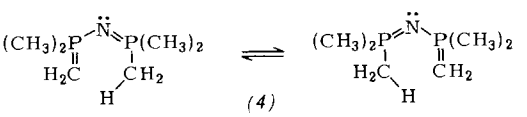
By *Hubert Schmidbaur* and *Hans-Joachim Füller*[*]

It has been reported that the salt-free trimethyl(methylene)-phosphorane *(2)* can be conveniently prepared by dehydrohalogenation of a tetramethylphosphonium salt *(1)* with sodamide in boiling tetrahydrofuran[1]. On carrying out this reaction in our laboratory, however, it has been established that this procedure is not free of side reactions and that, with suitable adjustment of the reaction conditions, the methylene-di-λ^5-phosphazene *(4)* is obtained in high yields. In addition to ammonia there is also methane evolved, which could be identified by gas chromatography.

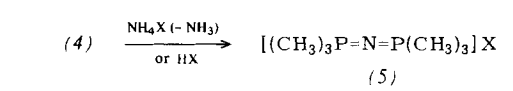
We suspect that the imide[2] *(3)* is formed as a precursor, since cleavage of hydrocarbons from phosphonium salts with alkali metal amide has been observed previously in at least two cases[3]. As a strong nucleophile, the anion of this precursor can then attack a second phosphonium center with cleavage of methane and formation of *(4)*. If the reaction is allowed to proceed at room temperature, instead of reflux temperature, the secondary reactions are (presumably for solubility reasons) more rapid than the primary formation of *(2)*, so the latter is continually being used up.



(4) is a pale yellow, highly reactive liquid which readily crystallizes on cooling. It follows from the ^1H-, ^{13}C-, and ^{31}P-spectra that this ylide is a fluctional compound; at elevated temperature the 17H, the 6C and the 2P atoms each are spectroscopically equivalent! The different positions of the atoms in the molecule can be differentiated only on strong cooling. This phenomenon can be interpreted only as the result of a rapid proton transfer[4], which in *(4)* proceeds both by an intramolecular and by an intermolecular mechanism[5]. The proton transfer in *(2)* is somewhat slower.



Reaction of acids or their ammonium salts[6] with *(4)* leads to the bis(trimethylphosphoranylidene)ammonium salts *(5)*, which were previously only accessible with difficulty *via* another route[2].



Like other ylides[7], *(4)* is an excellent complexing agent for numerous metal centers with which σ-bonded organometallic compounds can be synthesized. Thus, *e.g.*, reaction with trimethylgallium, like the corresponding reaction with *(2)*[9], leads initially to a 1 : 1 adduct *(6)*, m.p. 25—27 °C[8]. In contrast to $(CH_3)_3P—CH_2—Ga(CH_3)_3$, which can be distilled without decomposition[9], *(6)* loses methane on heating and yields the chelate *(7)*, m.p. 68—69 °C[8].

No corresponding precursor is detectable in the reaction of *(4)* with diethylzinc or dimethylcadmium—immediate formation of the chelates *(8)* and *(9)*, respectively, takes place (m.p. 75—77 and 86—88 °C, resp.[8]).

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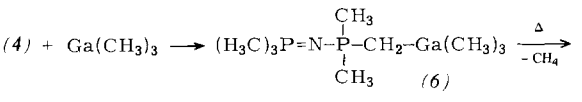
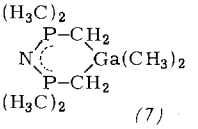
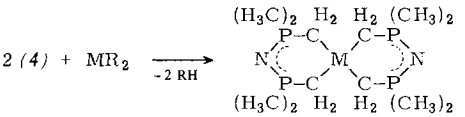


(6)



(7)

Accordingly, analogies can be drawn between *(4)* and acetylacetone and the isoelectronic bis(trimethylphosphoranylidene)methane[10].



(8), M = Zn, R = C_2H_5
(9), M = Cd, R = CH_3

Pentamethyl(methylene)di-λ^5-phosphazene (4)

Compound *(1)* (or the chloride) (68 g, 0.40 mol) is transferred to a suspension of $NaNH_2$ (22 g, 0.56 mol) in THF (750 ml). After 35 hours' stirring at 25 °C in the absence of air and moisture the reaction mixture is filtered and the filtrate fractionated *in vacuo*; after removal of *(2)* as a first fraction, there remains 22.4 g (68%) of *(4)*, b.p. 148–150 °C/30 torr, m.p. 14 °C. ^{1}H-NMR (in [D_8]-toluene at −60 °C, TMS ext.): δ = 1.19 (d, 9H, *J*(HCP) = 13.4 Hz), 1.37 (d, 6H, *J*(HCP) = 13.0 Hz), 0.10 (d, 2H, *J*(HCP) = 6.5 Hz). In {^{31}P} experiments three singlets (9:6:2) are obtained. At 80 °C all signals merge to a single broad singlet. ^{13}C-NMR (as above but at −20 °C, {^{1}H})[11]: δ = 18.0 (dd, 3C, *J*(CP) = 69.1, *J*(CPNP) ≈ 2.9 Hz), 24.2 (dd, 2C, *J*(CP) = 72.8, *J*(CPNP) ≈ 5.1 Hz), 10.0 (dd, 1C, *J*(CP) = 89.7, *J*(CPNC) ≈ 2.9 Hz). At higher temperature signal broadening and collapsing occurs. ^{31}P-NMR (as above but at −80 °C against H_3PO_4 ext., {^{1}H}): $\delta P^1 = 15.5$ (d, *J*(PNP) = 8.0 Hz), $\delta P^2 = 21.1$ (d). On warming signal broadening occurs.

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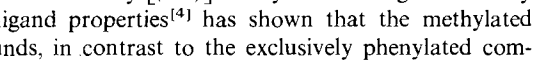
[9] *H. Schmidbaur, H.-J. Füller*, and *F. H. Köhler*, J. Organomet. Chem. *99*, 353 (1975).
[10] *H. Schmidbaur* and *O. Gasser*, J. Am. Chem. Soc. *97*, 6281 (1975); Angew. Chem. *88*, 542 (1976); Angew. Chem. Int. Ed. Engl. *15*, 502 (1976).
[11] We thank Priv.-Doz. Dr. *F. H. Köhler* and Frl. *G. Freitag* for these spectra.

The Ambident Ligand Properties of Bis(trimethylphosphoranylidene)methane

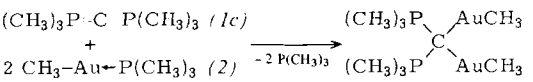
By *Hubert Schmidbaur* and *Oswald Gasser*[*]

Recently, more than ten years after the first synthesis of a "carbodiphosphorane" $R_3P{=}C{=}PR_3$ (with R = C_6H_5) by *Ramirez et al.*[1], we were able to prepare the partially [*(1a)*, *(1b)*][2] and the fully [*(1c)*] methylated analogs[3]. A study of the ligand properties[4] has shown that the methylated compounds, in contrast to the exclusively phenylated compound, show an ambident behavior and are thus novel chelating agents.

(1c) reacts with two equivalents of methyl(trimethylphosphane)gold[5] *(2)* with liberation of two equivalents of the phosphane to give a 1:2 complex, which on the basis of analytical and spectroscopic data can be assigned structure *(3)*.



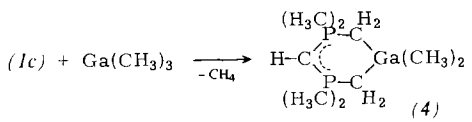
(1a), n = 1; *(1b)*, n = 2; *(1c)*, n = 3



(3)

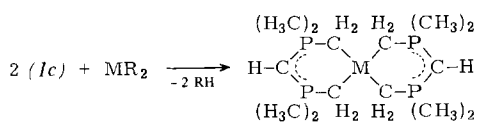
The colorless product *(3)*, which is air-sensitive, thermally stable up to 80 °C and soluble in organic solvents, is a new example of a molecule having two gold atoms bonded to a tetrahedrally coordinated C-atom[6].

In the reaction of equimolar amounts of *(1c)* and trimethylgallium, on the other hand, rapid evolution of methane already takes place slightly above room temperature, and the chelate *(4)* is formed.



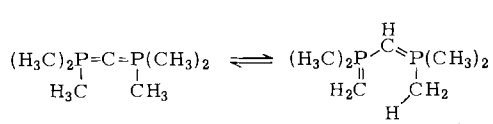
(4)

Finally, reaction of diethylzinc or dimethylcadmium with *(1c)* also proceeds with evolution of alkane, yielding the chelates *(5)* and *(6)*.



(5), M = Zn, R = C_2H_5;
(6), M = Cd, R = CH_3

(4), *(5)*, and *(6)* (m.p. 41, 85, and 84 °C, resp.) are colorless substances which are readily soluble in organic solvents and can be distilled unchanged *in vacuo*; their mass spectra show the molecular ion M^+ as an intense group of signals. Obviously the chelates *(4)*, *(5)*, and *(6)* are formed from the prototropic form *(1c')* of *(1c)*.



(1c) *(1c')*

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This ambident behavior is reminescent of the corresponding forms of acetylacetone, for each of which metal derivatives have been described[7]. The scope of the chemistry of the simply arylated carbodiphosphoranes[8] is thus significantly broadened. The present strong interest in ylide complexes[4] should therefore be further stimulated, as there are indications for practical uses in the literature[9].

Bis(methylgold)bis(trimethylphosphonio)methanediide (3)

A solution of *(1c)* (290 mg, 1.77 mmol) in ether (5 ml) is added dropwise at −60 °C in an inert atmosphere to a stirred solution of *(2)* (1.02 g, 3.54 mmol) in ether (10 ml). The mixture is then stirred for 1 h at 20 °C, filtered, and the precipitate washed with *n*-pentane and dried in a vacuum. The yield of *(3)* is almost quantitative. ^{1}H-NMR (in CH_2Cl_2, TMS ext.): δ(CH_3Au) = 0.55 (t, 6H, J(HCAuCP) = 1.2 Hz), δ(CH_3P) = 2.34 ($A_9XX'A'_9$, 18H, N = 12.2). ^{1}H-{^{31}P}: s, 6H; s, 18H.

Chelates (4), (5), and (6)

A suspension of *(1c)* (950 mg, 5.8 mmol) in benzene (10 ml) is treated with a solution of $Ga(CH_3)\cdot O(C_2H_5)_2$ (1.1 g, 5.8 mmol), $Zn(C_2H_5)_2$ (360 mg, 2.9 mmol), or $Cd(CH_3)_2$ (400 mg, 2.9 mmol) in benzene (10 ml). The reaction mixture is heated under reflux until evolution of gas (GLC: CH_4 or C_2H_6) is complete; the residue after removal of solvent is then distilled in a vacuum; yield *ca.* 80 % in each case. Complete ^{1}H-, ^{13}C-, and ^{31}P-NMR data are available for all three complexes. Example *(6)*: ^{1}H-NMR (in C_6D_6, TMS ext.): δ = 1.1 (d, 24H, $A_6XX'A'_6$, N = 10.9), −0.1 (d, 8H, $A_2XX'A'_2$, N = 12.0, ^2J(CdCH) = 34.5 Hz), −0.25 (m, 2H). {^{1}H}-^{13}C-NMR (in C_6D_6, C_6D_6 int. conv. to TMS): δ = 23.8 (m, 8C, AXX', N = 61.0), 2.6 (m, 4C, AXX', N = 48.8), 6.8 (t, 2C, ^1J(CH—P) = 119.6 Hz). {^{1}H}-^{31}P-NMR (in C_6H_6, H_3PO_4 ext.): δ = 13.2 (s, ^2J(CdCP) = 48.0 Hz).

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[2] *M. S. Hussain* and *H. Schmidbaur,* Z. Naturforsch. *31b,* 721 (1976).
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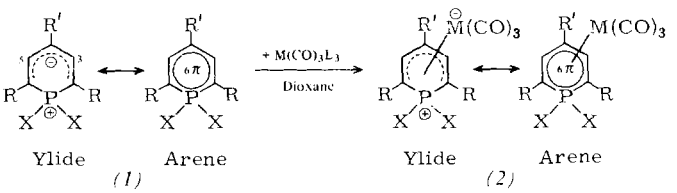
π-Complexes of λ^5-Phosphorins with Tricarbonylchromium, Tricarbonylmolybdenum, or Tricarbonyltungsten

By *Manfred Lückoff* and *Karl Dimroth*[*]

Dedicated to Professor Erich Hückel on the occasion of his 80th birthday

λ^5-Phosphorins *(1)* having hetero atoms or organic groups X linked *via* hetero atoms (O, N, S) at the P atom and aliphatic or aromatic groups R and R′ attached to the ring



(1) *(2)*

Table 1. Complexes *(2)* prepared.

Cpd.	X	R	R′	M	M.p. (dec.) [°C] (Yield [%] [a])	^{1}H-NMR, ^{31}P-NMR, and ^{19}F-NMR [ppm]; IR [cm^{-1}]; [b]
(2a)	OCH_3	C_6H_5	C_6H_5	Cr	193—196 (52)	6.35 (2H, d, $^3J_{P-H}$ = 28 Hz); 3.75 (3H, d, $^3J_{P-H}$ = 9 Hz); 3.6 (3H, d, $^3J_{P-H}$ = 14 Hz); ^{31}P: δ = −37.79; IR: 1935, 1870, 1830
(2b)	OCH_3	C_6H_5	C_6H_5	Mo	197—203 (6)	6.72 (2H, d, $^3J_{P-H}$ = 26.3 Hz); 3.78 (3H, d, $^3J_{P-H}$ = 9.5 Hz); 3.75 (3H, d, $^3J_{P-H}$ = 13.5 Hz); IR: 1950, 1885, 1845
(2c)	OCH_3	C_6H_5	C_6H_5	W	above 213 (7)	6.5 (2H, d, $^3J_{P-H}$ = 23.2 Hz); 3.85 (3H, d, $^3J_{P-H}$ = 14.8 Hz); 3.74 (3H, d, $^3J_{P-H}$ = 12.3 Hz); IR: 1935, 1865, 1825
(2d)	OCH_3	C_6H_5	CH_3	Cr	190—193	6.03 (2H, d, $^3J_{P-H}$ = 28 Hz); 3.68 (3H, d, $^3J_{P-H}$ = 10 Hz); 3.57 (3H, d, $^3J_{P-H}$ = 14 Hz); 2.3 (3H, d, $^5J_{P-H}$ = 2 Hz); ^{31}P: δ = −34.41; IR: 1930, 1850, 1810
(2e)	OCH_3	C_6H_5	$CH_2—C_6H_5$	Cr	192—195 (60)	6.12 (2H, d, $^3J_{P-H}$ = 28 Hz); 3.95 (2H, s); 3.76 (3H, d, $^3J_{P-H}$ = 11 Hz); 3.52 (3H, d, $^3J_{P-H}$ = 14 Hz); ^{31}P: δ = −35.08; IR: 1945, 1870, 1840,
(2f)	OCH_3	C_6H_5	$C(CH_3)_3$	Cr	185—189 (58)	6.2 (2H, d, $^3J_{P-H}$ = 28 Hz); 3.77 (3H, d, $^3J_{P-H}$ = 11 Hz); 3.64 (3H, d, $^3J_{P-H}$ = 14 Hz); 1.46 (9H, s); ^{31}P: δ = −35.29; IR: 1915, 1840, 1825
(2g)	OCH_3	C_6H_5	phthalimido	Cr	150—155 (55)	6.28 (2H, d, $^3J_{P-H}$ = 27 Hz); 3.76 (3H, d, $^3J_{P-H}$ = 10 Hz); 3.70 (3H, d, $^3J_{P-H}$ = 14 Hz); ^{31}P: δ = −32.26; IR: 1960, 1890, 1870, 1735
(2h)	F	C_6H_5	C_6H_5	Cr	152—156 (53)	6.92 (2H, oct, $^3J_{P-H}$ = 35 Hz, $^4J_{F-H}$ = 6 Hz and 2 Hz); ^{31}P: δ = −35.65 ($^1J_{P-F}$ = 1352 and 954 Hz); ^{19}F: δ = −2.93 and −107.96 ($^1J_{P-F}$ = 1344 and 954 Hz); IR: 1985, 1925, 1890
(2i)	F	C_6H_5	$C(CH_3)_3$	Cr	123—125 (45)	6.48 (2H, oct, $^3J_{P-H}$ = 36 Hz, $^4J_{F-H}$ = 6 Hz and 2 Hz); 1.52 (9H, s); ^{31}P: δ = −35.46 ($^1J_{P-F}$ = 1346 and 954 Hz); ^{19}F: δ = −2.32 and −109.2 ($^1J_{P-F}$ = 1346 and 955 Hz); IR: 1960, 1885, 1860

[a] Yields based on the isolated pure compounds, not optimized.
[b] All spectra in [D_6]-acetone relative to TMS (^{1}H-NMR), 85 % H_3PO_4 (^{31}P-NMR), or $CFCl_3$ (^{19}F-NMR). Negative signs imply downfield shifts relative to the standard only in the case of the ^{31}P-NMR spectra. Absorption signals of the aromatic protons in the ^{1}H-NMR spectra are not included in the table. IR in KBr or in cyclohexane.

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atoms C-2, C-6, and C-4 resemble electron-rich 6π-delocalized arenes more closely than 6π-delocalized ylides in their chemical[1] and physical[2] properties. We have now synthesized the first π-complexes *(2)* of such phosphorins with tricarbonylchromium, tricarbonylmolybdenum, and tricarbonyltungsten (Table 1).

All the new complexes, which were obtained as air-stable orange-red to yellow crystals by heating *(1)* with $M(CO)_6$ or $M(CO)_3(CH_3CN)_3$ in dioxane or benzene, afford correct elemental analyses. In their mass spectra the M^+ peak rarely lies above 15%; loss of CO and $M(CO)_3$ is observed.

In each case the upfield shift of the protons at C-3 and C-5 in the ^{1}H-NMR spectra demonstrate that the central λ^5-phosphorin and not one of the peripheral phenyl groups is the actual π-donor. On complex formation to give *(2)* the equivalent groups X in *(1)* (OCH_3 or F) acquire different chemical environments. The signal of the ^{31}P nucleus undergoes only a relatively slight upfield shift on complexation, whereas in the λ^3-phosphorin-carbonylchromium complexes the upfield shift is large[3,4]. The carbonyl groups attached to the metal atom can be recognized from their IR absorption, both in cyclohexane solution and in KBr (see Table 1).

X-Ray structure analysis[5] of *(2a)* and *(2i)* shows that the λ^5-phosphorin ring remains planar on complexation. The P—Cr distance is relatively long in *(2a)*. It becomes significantly shorter on replacement of the OCH_3 groups on the phosphorus by F atoms and the phenyl group at C-4 by the *tert*-butyl group [compound *(2i)*]. This is due to both steric and electronic reasons because the distances P-(C-2)= P-(C-6) are also smaller in *(2i)* than in *(2a)*. No X-ray structure analysis of a typical tricarbonylchromium-ylide complex[6] is yet available. Thus it is not possible to decide to what extent the ylide form or the arene form participate more significantly in the ground state bonding of the λ^5-phosphorin-carbonylmetal complexes *(2)*.

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German version: Angew. Chem. 88, 543 (1976)

CAS Registry numbers:
(2a), 59821-84-0; *(2b)*, 59821-86-2; *(2c)*, 59821-87-3; *(2d)*, 59821-88-4; *(2e)*, 59821-89-5; *(2f)*, 59821-90-8; *(2g)*, 59821-91-9; *(2h)*, 59821-92-0; *(2i)*, 59821-85-1

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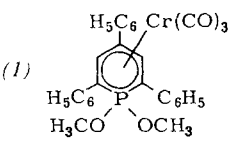
X-Ray Structure Analysis of Two π-Complexes of λ^5-Phosphorins with Tricarbonylchromium

By *Tony Debaerdemaeker*[*]

Dedicated to Professor Erich Hückel on the occasion of his 80th birthday

We have performed X-ray structure analyses of the tricarbonylchromium complexes of 1,1-dimethoxy-2,4,6-triphenyl-λ^5-phosphorin *(1)*[1] and of 4-*tert*-butyl-1,1-difluoro-2,6-diphenyl-λ^5-phosphorin *(2)*[1].

(1)



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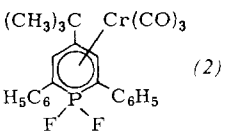

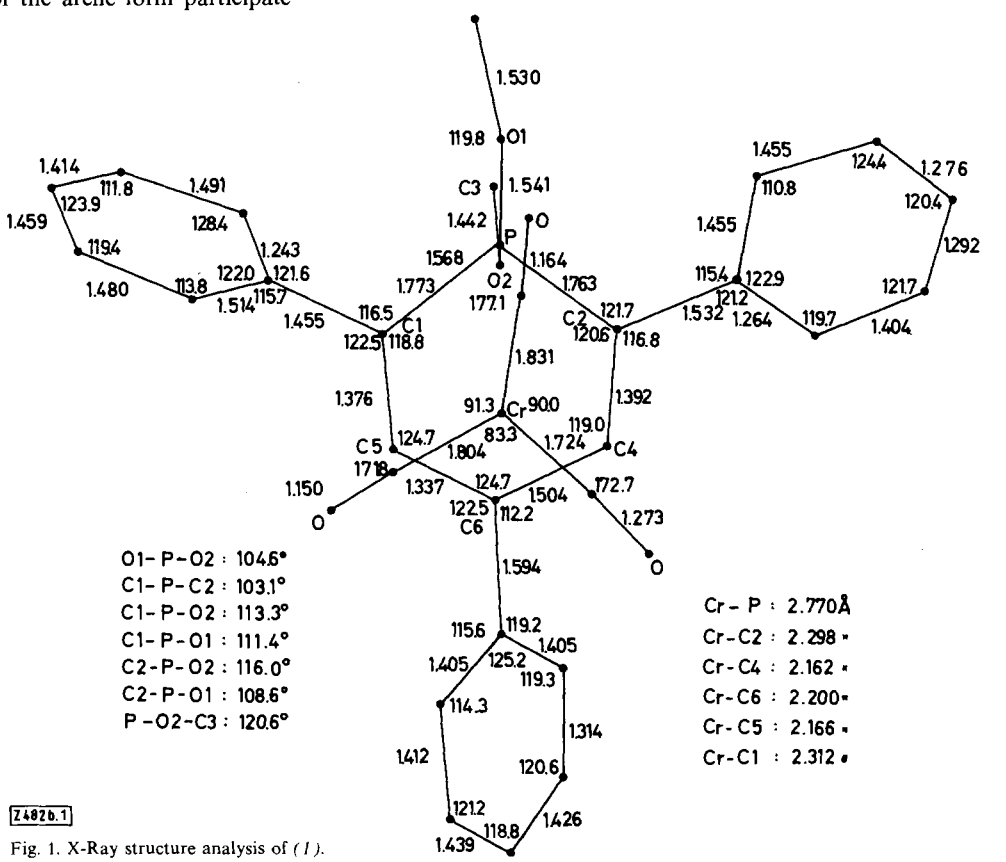

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Fig. 1. X-Ray structure analysis of *(1)*.

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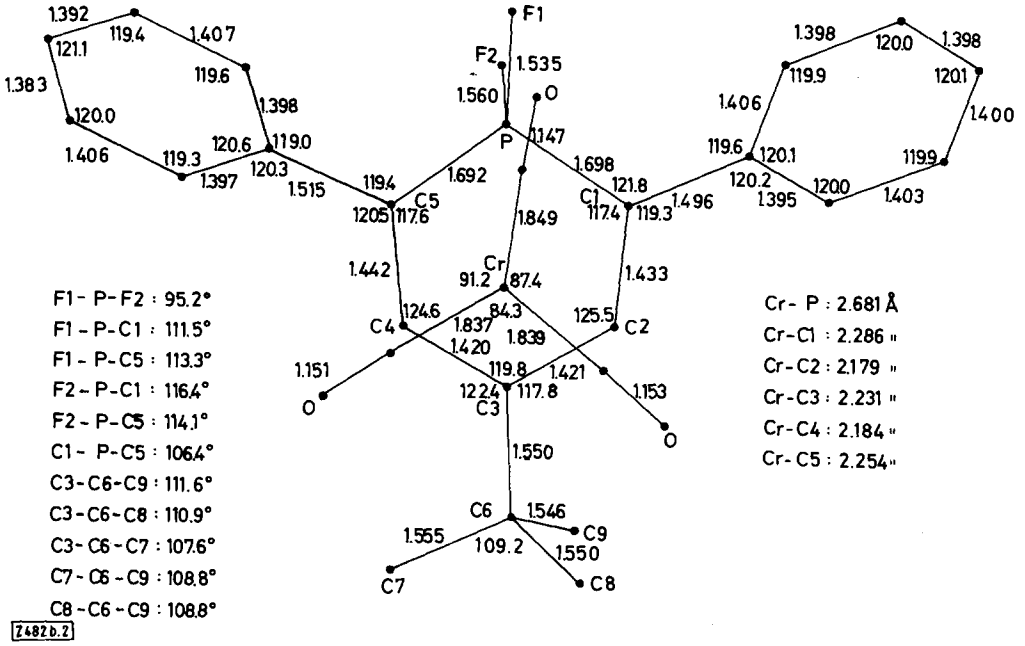

Fig. 2. X-Ray structure analysis of *(2)*.

Compound *(1)* crystallizes in the orthorhombic space group $P2_12_12_1$ with $a=18.655$, $b=15.550$, $c=8.529$ Å, $Z=4$; complex *(2)* crystallizes in the monoclinic space group $P2_1/a$ with $a=15.092$, $b=12.442$, $c=13.119$ Å, $\beta=115.08°$, $Z=4$. The reflections of the two crystals were recorded on an automatic Philips four-circle diffractometer (Mo-Kα radiation). The two structures were solved by direct methods (MULTAN[2]). Refinement with anisotropic temperature factors led to a final value of $R=11.4\,\%$ and $5.9\,\%$ respectively. All the results of importance are to be seen in the two Figures (distances given in Å).

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CAS Registry numgers:
(1), 59821-84-0; *(2)*, 59821-85-1

[1] Synthesis: *M. Lückoff* and *K. Dimroth*, Angew. Chem. *88*, 543 (1976); Angew. Chem. Int. Ed. Engl. *15*, 503 (1976). Complexes *(1)* and *(2)* are designated as *(2a)* and *(2i)*, respectively, in ref. [1].

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α,α-Doubly Deprotonated Nitroalkanes. Enhancement of the C-Nucleophilicity of Nitronates[**]

By *Dieter Seebach* and *Friedrich Lehr*[*]

Nitronates *(1)* are synthetically versatile components when it is remembered that the products *(2)* formed by C—C linkage with electrophiles can be converted by reduction into amines [see *(1a)*] and by Nef reaction into carbonyl compounds [see *(1b)*].

Unfortunately, the nucleophilic strength of the C atom located α to the N atom of *(1)* leaves much to be desired[1]: alkylations (except with nitrobenzyl halides or as intramolecu-

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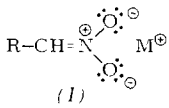
Table 1. α-Nitro esters and ketones, α-nitro(phenylthio)alkanes, and β-nitro alcohols as products *(2)* [a] of dianion derivatives *(4)* and carboxylic esters and anhydrides and acyl chlorides, as well as alkyl halides, aldehydes, and ketones. Yields not optimized. The NMR spectra were recorded on a Varian T 60 instrument with TMS as internal standard.

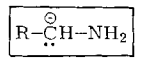
$[R—\underset{(4)}{C}=NO_2]^{2\ominus}\,2Li^{\oplus}$ + Electrophile → $\underset{(2)}{RCHE—NO_2}$

No.	R	Electrophile [E in *(2)*]	Yield [%]	^{1}H-NMR [b]
1	H	Diethyl carbonate [C_2H_5OCO]	65	5.1, s
2	C_2H_5	Dimethyl carbonate [CH_3OCO]	55	4.9, t (7)
3	$(CH_3)_2CH$	Methyl chloroformate [CH_3OCO]	65	4.8, d (8)
4	n-C_4H_9	Dimethyl carbonate [CH_3OCO]	65	5.0, t (8)
5	$(CH_3)_2CH$	Acetic anhydride [CH_3CO]	30	4.8, d (8)
6	$(CH_3)_2CH$	Methyl butyrate [n-C_3H_7CO]	60	4.8, d (9)
7	$(CH_3)_2CH$	Methyl isobutyrate [$(CH_3)_2CH—CO$]	75	5.0, d (8)
8	$(CH_3)_2CH$	Methyl benzoate [C_6H_5CO]	75	5.7, d (8)
9	C_6H_5S	1-Bromopentane [n-C_5H_{11}]	70	5.3, t (7)
10	C_6H_5S	1-Iodohexane [n-C_6H_{13}]	75	5.3, t (7)
11	C_2H_5	Benzaldehyde [$C_6H_5CH(OH)$]	80 [c]	4.4, dt (4/10)
12	C_6H_5S	Benzaldehyde [$C_6H_5CH(OH)$]	80 [c]	5.3, m
13	C_2H_5	Acetone [$(CH_3)_2C(OH)$]	40	4.3, dd (4/12)
14	C_2H_5	Cyclohexanone [$(CH_2)_5C(OH)$]	65	4.2, dd (4/10)
15	C_2H_5	Benzophenone [$(C_6H_5)_2C(OH)$]	65	5.3, dd (4/11)

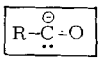
[a] For the known products (nos. 1—4, 13, 14) the physical data recorded agree with values given in the literatur [1, 4].
[b] δ-values [ppm], multiplicity and coupling constant [Hz] of the α-nitro protons.
[c] Diastereomeric mixture.



(1)



(1a)



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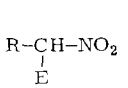

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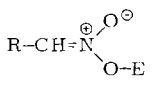
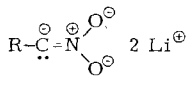


(3)



(4)

lar reaction) and acylations (except with methoxymethylmagnesium carbonate or acyl cyanides) afford the *O*-derivatives *(3)*, and the nitroaldol reaction [*(1)*→*(2)*, E=R'R''C(OH)] becomes less and less satisfactory the more substituents there are attached to the C atoms to be linked together.

We have found that this situation is open to improvement: addition of two equivalents of *n*-butyllithium (1.6 molar in *n*-hexane) to a solution of a nitroalkane (10 mmol) in THF/HMPT (50 ml/10 ml) stirred at −90 °C[2] leads to dilithium derivatives *(4)* (with $R=C_2H_5$ stable up to −30 °C) whose C-nucleophilicity is drastically enhanced relative to that of *(1)*. Thus the adduct *(2)*, $R=(CH_3)_2CH$, $E=C_6H_5CO$, is obtained by successive addition of one equivalent of methyl benzoate and 2.5 equivalents of HCl (in THF) to *(4)*, $R=(CH_3)_2CH$, at −90 °C. A control experiment with the nitronate *(1)*, $M^{\oplus}=Li^{\oplus}$, generated with one equivalent of butyllithium failed to give any product *(2)* under otherwise identical conditions.

The examples listed in Table 1 show: a) double deprotonation to give *(4)* is successful with a wide range of nitroalkanes (nos. 1—4, 9)[3]; b) the doubly metalated nitroalkanes *(4)* can be *C*-acylated with carboxylic acid derivatives to give α-nitro carbonyl compounds (nos. 1—8); c) *C*-alkylation can be accomplished with *(4)*, $R=SC_6H_5$ (nos. 9, 10); d) the nitroaldol reaction, also possible *via* simple nitronates *(1)* with base catalysis, *e.g.* with aminoethanol[1], proceeds in better yields with *(4)*, especially in cases of steric hindrance (nos. 11—15).

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CAS Registry numbers:
(2) ($R=C_2H_5$, $E=CH_3OCO$), 59906-50-2;
(2) ($R=(CH_3)_2CH$, $E=CH_3OCO$), 40149-55-1;
(2) ($R=n$-C_4H_9, $E=CH_3OCO$), 59906-51-3;
(2) ($R=(CH_3)_2CH$, $E=CH_3CO$), 59906-52-4;
(2) ($R=(CH_3)_2CH$, $E=n$-C_3H_7CO), 59906-53-5;
(2) ($R=(CH_3)_2CH$, $E=(CH_3)_2CH—CO$, 59906-54-6;
(2) ($R=(CH_3)_2CH$, $E=C_6H_5CO$, 59906-55-7;
(2) ($R=C_6H_5S$, $E=n$-C_5H_{11}), 59906-56-8; *(2)* ($R=C_6H_5S$, $E=n$-C_6H_{13}), 59906-57-9; *(2)* ($R=C_2H_5$, $E=C_6H_5CH(OH)$), isomer A, 59906-58-0; *(2)* ($R=C_2H_5$, $E=C_6H_5CH(OH)$), isomer B, 59906-59-1; *(2)* ($R=C_6H_5S$, $E=C_6H_5CH(OH)$), isomer A, 59906-60-4; *(2)* ($R=C_6H_5S$, $E=C_6H_5CH(OH)$), isomer B, 59906-61-5; *(2)* ($R=C_2H_5$, $E=(CH_3)_2C(OH)$), 59906-62-6;
(2) ($R=C_2H_5$, $E=(CH_2)_5C(OH)$), 59906-63-7;
(2) ($R=C_2H_5$, $E=(C_6H_5)_2C(OH)$), 51686-89-6;
(4) (R=H), 59906-64-8; *(4)* ($R=C_2H_5$), 59906-65-9;
(4) ($R=(CH_3)_2CH$), 59906-66-0; *(4)* ($R=n$-C_4H_9), 59906-67-1;
(4) ($R=C_6H_5S$), 59906-68-2; dimethyl carbonate, 616-38-6; methyl chloroformate, 79-22-1; acetic anhydride, 108-24-7; methyl butyrate, 623-42-7; methyl isobutyrate, 547-63-7; methyl benzoate, 93-58-3; 1-bromopentane, 110-53-2; 1-iodohexane, 638-45-9; benzaldehyde, 100-52-7; acetone, 67-64-1; cyclohexanone, 108-94-1; benzophenone, 119-61-9

[1] See references in: *O. von Schickh, G. Apel, H. G. Padeken, H. H. Schwarz,* and *A. Segnitz* in Houben-Weyl-Müller: Methoden der Organischen Chemie, Vol. X/1; Thieme, Stuttgart 1971; *H. Feuer* in *S. Patai*: The Chemistry of the Nitro- and Nitroso Groups, Parts 1 and 2. Interscience-Wiley, New York 1969/70.

[2] The reactions become very unclear at higher temperatures *A. K. Hoffmann, A. M. Feldman,* and *E. Gelblum*, J. Am. Chem. Soc. *86*, 646 (1964); *S. Wawzonek* and *J. V. Kempf*, J. Org. Chem. *38*, 2763 (1973).

[3] a) The double deprotonation of 1-aryl-2-nitroethanes proceeds in a different manner; *R. Henning, F. Lehr,* and *D. Seebach*, Helv. chim. Acta *59* (1976), in press; b) nitro(phenylthio)methane ($n_D^{28}=1.5768$) was prepared from C_6H_5SCl and the Na salt of nitromethane.

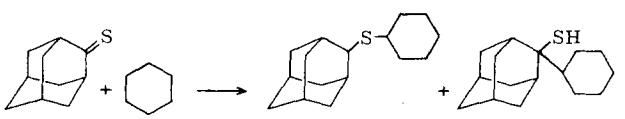
[4] *W. Steinkopf*, Justus Liebigs Ann. Chem. *434*, 21 (1923).

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

The photochemistry of thiones and the chemistry of the S_2 state are considered by *P. de Mayo*. Thiones can react both in higher and in lower states. Cycloadditions of thiones in the T_1 state are not stereospecific, but do appear to be more regiospecific than for the corresponding ketones. Reactions of the S_2 state in solution have so far only been reported for thiones among the simple chromophores. They formally involve nonregiospecific insertions into CH bonds. A relevant example is the reaction of adamantanethione *(1)* with cyclohexane. The addition of *(1)* to olefinic double bonds does not appear to be regiospecific, but instead stereospecific.



(1)

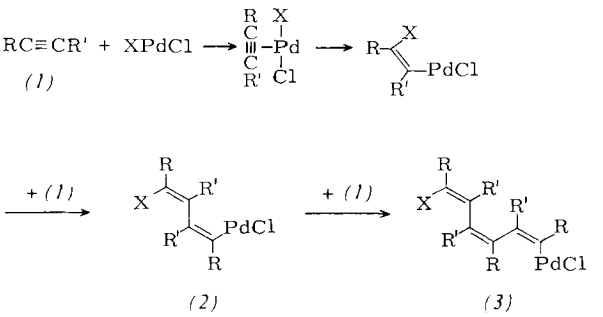
Thiones in the S_2 state accordingly behave in the same way as carbenes. [Thione Photochemistry, and the Chemistry of the S_2 State. Acc. Chem. Res. *9*, 52—59 (1976); 67 references]
[Rd 863 IE—L]

The structure and significance of β_2-microglobulin is reported by *B. A. Cunningham*. Particularly important is the finding that this protein is homologous in its amino sequence with the constant regions of both classes of light chains of the immunoglobulins as well as the constant homology regions of at least three of the heavy chains. β_2-Microglobulins are also found in other vertebrates apart from man. The gene for β_2-microglobulin was probably formed from a precursor which gave cause for formation of the light and heavy chains of the immunoglobulins by duplication. From the wide distribution of β_2-microglobulin on the surface of various cell types it can be expected that the results of analysis of the immunosystem can also be applied to other areas of cell biology. In particular, the connection between β_2-microglobulin and the histocompatibility antigens permits conclusions on the origin, structure, and function of these and other cell surface proteins. [Structure and Significance of β_2-Microglobulins. Fed. Proc. *35*, 1171—1176 (1976); 39 references]
[Rd 872 IE—R]

ESCA investigations on industrial catalysts form the theme of a report by *J. S. Brinen*. By ESCA (Electron Spectroscopy for Chemical Analysis) it can be established which elements a surface consists of, which atoms or compounds are chemically bound to it, and which physical and chemical changes accompany the catalytic reaction. The fundamental principles of electron spectroscopy and an outline of sample preparation are followed by a discussion of possible applications *e.g.* investigations on the distribution of promoters (Mo, Co, P), on the carrier material (Al_2O_3), and on the dispersion of metal atoms (Rh/C catalyst). The charging of semi- and nonconductors by the photoelectronic process is also discussed. [Applying Electron Spectroscopy for Chemical Analysis to Industrial Catalysis. Acc. Chem. Res. *9*, 86—92 (1976); 13 References]

[Rd 866 IE—L]

The palladium(II)-induced oligomerization of acetylenes *(1)* is reported by *P. M. Maitlis*. The bis(benzonitrile) complex of palladium chloride is commonly used as catalyst. The reaction proceeds with stepwise *cis*-insertion of the acetylenes in Pd—Cl and Pd—C bonds. Benzene derivatives are formed from *(2)* *via* cyclobutadiene- and from *(3)* *via* cyclopentadienylmethyl-



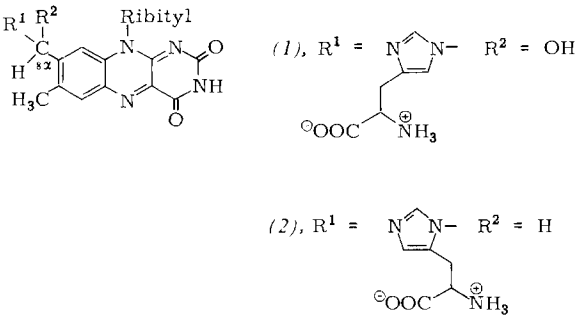
palladium complexes. The route which the reaction finally takes depends on the size and type of substituents R and R'. [The Palladium(II)-Induced Oligomerization of Acetylenes: An Organometallic Detective Story. Acc. Chem. Res. *9*, 93—99 (1976); 45 References]

[Rd 867 IE—L]

The use of cyclic peptides for conformational studies is reviewed by *C. M. Deber, V. Madison*, and *E. R. Blout*. Cyclic peptides containing proline and glycine fulfill the requirements of model compounds which unite biological importance and simple structure. An example is *cyclo*(-Pro-Gly-)$_3$. From the measured ^{13}C-NMR, ^{1}H-NMR, and CD spectra of such peptides and the calculated CD spectra and conformation energies it can be ascertained *e.g.* whether the X-Pro bonds are *cis*- or *trans*-configurated and how the conformation changes in the presence of cations. [Why Cyclic Peptides? Complementary Approaches to Conformations. Acc. Chem. Res. *9*, 106—113 (1976); 45 References]

[Rd 868 IE—L]

8α-Substituted flavins of biological importance are dealt with in an article by *D. E. Edmonson* and *T. P. Singer*. The compound previously believed to be the 8α-histidine-substituted 8α-hydroxyriboflavin *(1)* has now turned out to be the riboflavin with an isomeric 8α-histidine grouping *(2)*. This finding calls for further discussion of some reaction mechanisms. Moreover,



new findings on covalently bound flavins have opened the way to some interesting possible applications. [8α-Substituted Flavins of Biological Importance: an Updating. FEBS Lett. *64*, 255—265 (1976); 52 references]

[Rd 870 IE—R]

Isolation, properties and distribution of β_2-microglobulins form the theme of an article by *I. Berggård*. These proteins are identical with the light chains of the histocompatability (HL-A) antigens. They may be readily isolated from the urine of individuals whose kidney exhibits a resorption defect. Physicochemical and chemical investigations show that they are very similar in amino acid composition as well as secondary and tertiary structure to isolated immunoglobulin domains. They occur in free form in various body fluids as subunits of the HL-A antigens on cell surfaces. However, a part also appears to be bound to the cell surface in some other way, since the number of the β_2-microglobulin molecules exceeds that of the HL-A antigens. [β_2-Microglobulins. Isolation, Properties, and Distribution. Fed. Proc. *35*, 1167—1170 (1976); 49 references]

[Rd 873 IE—R]

Environmental factors in drug metabolism are discussed in a review by *J. R. Gilette*. Although the activity of the cytochrome-P-450 enzyme is subject to external factors *in vitro*, the pharmacokinetics in the living animal is not necessarily influenced in the expected sense. Still other factors play a role here, such as the influence on elimination mechanisms; even the type of application or the breed of the experimental animal are of significance. Hence one cannot draw conclusions about the influence of environmental factors on drug metabolism in intact animals from *in vitro* experiments. [Environmental Factors in Drug Metabolism. Fed. Proc. *35*, 1142—1147 (1976); references]

[Rd 874 IE—R]

BOOK REVIEWS

Quantum Mechanics for Organic Chemists. By *H.-E. Zimmerman*. Academic Press, New York—San Francisco—London 1975. 1st edit., x, 215 pp., numerous figs., bound, $ 16.50.

This book provides an introduction to the methods of MO theory.

The main emphasis in the book is placed on Hückel theory, despite the title's broader connotations. In Chapter 1 this theory is developed by means of procedures for the determination of orbital energies and LCAO-MO coefficients, this approach rapidly leading up to a level of knowledge at which

questions of chemical importance can be treated. Quantum-mechanical principles are added in Chapter 2. Use of symmetry as a calculation aid in Chapter 3 steers the reader towards the formal methods of group theory. Here again we note the basic concept of the book, *i.e.* its intention to ease the organic chemist's entry into theory: the terminology and the instructions for use are introduced before the presentation of formal theory. Chapter 4 considers in brief variants of the Hückel theory and its application to alternant and nonalternant hydrocarbons and to correlation diagrams. Greater detail is devoted to hybrid orbitals. Advanced MO procedures and methods of configurational interaction are outlined in Chapter 5.

An important feature of the book is the detailed working of examples, so that the reader becomes familiar with the methods by the paper-and-pencil method; this is supported by setting up problems and their solution. The detailed presentation of solutions, however, means a diminished amount of material, whose selection reflects the author's field of work, *e.g.* Möbius systems. Unfortunately, some concepts such as wave function and charge density, or eigenvalue and expectation value, are not always sufficiently differentiated. A few incorrect formulas and expressions should be corrected.

Franz Mark [NB 316 IE]

Radio-Immunoassay of Steroid Hormones. Edited by *D. Gupta*. Verlag Chemie, GmbH, Weinheim 1975. 1st edit., xiv, 224 pp., 56 figures, 53 tables, linen, DM 58.—.

Part of this book presents the proceedings of a workshop held by the German Endocrine Society in February, 1974. In addition, other authors have contributed further chapters, so that assay methods for all the clinically important steroid hormones have been included. The intention of the book, as stated in the Foreword, was to "review the present state of the art of steroid radioimmunoassay", and in this respect the delay in the appearance of the book can only be regretted.

The topics covered include discussions of the basic principles of radioimmunoassay. These tend to be rather cursory, and are intended for workers already familiar with radioimmunoassay procedures. This volume would have been of increased value if more of the chapters concerning specific assay methods had also contained some discussion of the general problems concerning the assay of that steroid, and some comparative evaluation of the previously published radioimmunoassay methods. However, some chapters provide the reader with a broader insight into the subject matter; those devoted to the discussion of the assay of steroid glucuronides, and of the use of ^{125}I tracers for steroid determination.

It is difficult to decide which readership this volume is intended for—the expert, the clinician, the laboratory worker, or the total beginner. It follows the trend of recent book publications on radioimmunoassay; collecting together a series of methods from workers in this field and attempting to knit them into a comprehensive review. The lack of overall editorial unity in the presentation is regrettable.

E. Jean Wickings [NB 325 IE]

Raman/IR Atlas organischer Verbindungen (Raman/IR atlas of organic compounds). Edited by *B. Schrader* and *W. Meier* on behalf of the Institut für Spektrochemie und Angewandte Spectroskopie, Dortmund. Verlag Chemie, GmbH, Weinheim. 3 instalments in 2 loose-leaf files. 1st instalment 1974, xxxi, 314 pp. with 314 spectra; 2nd instalment 1975, xlii, 344 pp. with 301 spectra. Price per instalment DM 265.— (purchase of complete work is a condition of sale).

The Raman/IR Atlas covers about 1000 organic compounds, divided into 15 principal groups and 93 classes. The authors have taken pains to provide a representative selection of substances.

On each A4 page of the work the IR/FIR and the Raman spectrum of the relevant substance are reproduced together with details of instrumentation (instrument, cell material, preparation technique, spectral slit width, *etc.*) and substance parameters (molecular formula, molecular mass, degree of purity, melting and boiling point).

The spectra of the 1st instalment are redrawn by hand from the original spectra; those of the 2nd instalment are recorded in digital form, computer corrected with respect to the spectral sensitivity of the Raman spectrometer, and subsequently plotted out. Each volume closes with a list of spectra and a formula index.

The quality of the spectra and of their reproduction is excellent. The volumes are very useful compendia of spectra for all those concerned with Raman and IR spectra in research and teaching.

Egon Fahr [NB 326 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Datemsammlung zur Toxikologie der Herbizide. Edited by the "Arbeitsgruppe Toxikologie" der Kommission für Pflanzenschutz-, Pflanzenbehandlungs- und Vorratsschutzmittel der Deutschen Forschungsgemeinschaft, 2nd instalment. Verlag Chemie, Weinheim 1976. Loose-leaf, DM 98.00.

Elektrochemische Bauelemente. By *A. F. Bogenschütz* and *W. Krusemark*. Verlag Chemie, Weinheim 1976. ix, 247 pp., bound, DM 145.00.

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Collisional Activation Mass Spectrometry—A New Probe for Determining the Structure of Ions in the Gas Phase[**]

New analytical methods (7)

By Karsten Levsen and Helmut Schwarz[*]

Organic ions with high translational energy colliding inelastically with neutral atoms or molecules become excited electronically at the expense of their translational energy. The excitation energy enables a wide range of dissociation reactions to occur and the intensity relationships yield information about the structure of the ions concerned and also permit conclusions to be drawn about the mechanism of their formation.

1. Introduction

Mass-spectrometric investigations are affected in many cases by the occurrence of collision-induced processes involving the residual gas so that often, *e.g.* in the study of metastable ions, considerable effort is necessary to eliminate the influence of these collision processes. Only during the last eight years has it been shown by the systematic investigations by *McLafferty*[1], *Jennings*[2] and *Beynon*[3, 4] that these processes, originally considered a nuisance, can in fact provide a wealth of information. The above authors concentrated on the one hand on charge-transfer reactions[4] and on the other hand on collision-induced dissociation processes[1–3, 5, 6]. In the course of this work it became clear that these collision-induced dissociation processes—to which the present article is confined—provide valuable information about organic ions, for example about their physical properties, their structures[*], and the mechanisms of their formation and decomposition. Further, analytical applications become apparent for the determination of the structure of organic compounds and for analysis of mixtures. In what follows the theoretical principles of collision-induced dissociation and the methods of measurement are first described, followed by presentation of the applications.

2. Theoretical Principles

2.1. Energy Transfer

When ions having a high translational energy (a few hundred eV or more) collide inelastically with neutral atoms or molecules, part of their translational energy is converted into excitation energy of the ions which can subsequently lead to the latter's decomposition. A collision-induced dissociation of this kind can also be called a dissociative ion-molecule reaction [in accordance with eq. (a)].

$$[m_1]^+ + N \rightarrow [m_2]^+ + [m_3] + N \qquad (a)$$

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[**] Abbreviations: CA: collisional activation; CI: chemical ionization; CID: collision-induced dissociation; DADI: direct analysis of daughter ions; EA: electron attachment; EI: electron impact ionization; FD: field desorption; FI: field ionization; ICR: ion cyclotron resonance; *MI*: metastable ions; *SID*: surface-induced dissociation; MIKE: mass analyzed ion kinetic energy.

[*] The term "structure" refers here solely to the bonding of atoms. Bond lengths, bond angles, configurational or conformational differences, and electron-density distributions, are left out of account. Thus, "structure" is here equivalent to "constitution".

The whole group of fragments of a given primary ion produced by collision is known as the collisional activation (CA) spectrum of this ion[1][*]. If fragment-ions rather than molecular ions are investigated, then the CA spectrum is in some respects the mass spectrum of a fragment.

When the translational energy exceeds 1 keV and the colliding gas atoms are small, the first process that takes place is mainly electronic excitation of the impacting ion[7]. This electronic excitation is converted into vibrational excitation which rapidly (within a few picoseconds) distributes itself statistically over the whole ion and can lead to the rupture of specific bonds. Since the energy-transfer mechanism corresponds to that in the collision of an electron with a neutral molecule in the ion source of a mass spectrometer, it can be described by the quasi-equilibrium theory (QET)[8]. The analogous energy-transfer mechanism is also the reason why the electron impact and the collisional-activation spectra of a molecular ion show the same fragments[1,2,6,9]. This does not necessarily imply that the internal energy distribution in a molecular ion must be the same after collision with electrons and atoms, since this energy distribution is a function of the kinetic energy of the electrons or ions. However, the relative fragment intensities in 70 eV electron impact spectra are very similar to those obtained in collisional-activation spectra of the same molecular ions with 8—10 keV ions[1,2,9], and this makes it probable that the energy distributions are often comparable. In both cases a broad spectrum of excitation energies (0—10 eV) is produced; in collisional activation the energy distribution *after* the collision is only slightly influenced by the energy distribution *prior to* the collision[1c]. The similarity between the collisional-activation spectra and the 70-eV electron impact spectra is due not only to a similar energy distribution but also to a comparable decomposition time, which for instrumental reasons is around 10^{-6} sec in both cases.

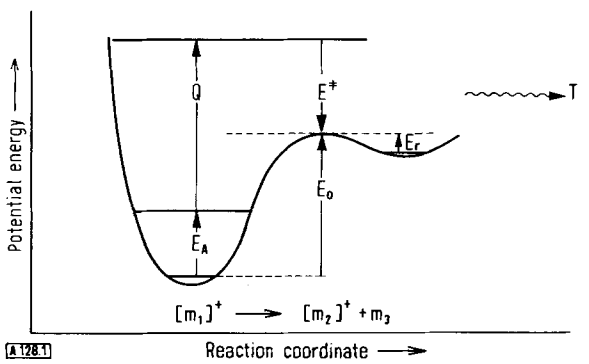


Fig. 1. Energy transfer in collision-induced dissociation. Let the primary ion $[m_1]^+$ have a mean excitation energy E_A before the collision. On inelastic collision an amount Q of the translational energy is converted into internal energy. After overcoming an activation threshold E_0 the excited ion decomposes into a fragment ion $[m_2]^+$ and a neutral particle m_3. The excess ("non-fixed") energy E^+ and the activation energy of the reverse reaction E_r are released partly as translational energy T (signal broadening). (The kinetic shift is left out of account for the sake of clarity.)

The excitation energy that the ion gains in the collision is of the same magnitude as the loss of its translational energy. (The fraction of kinetic energy transferred to the target atom is negligible[*].) The decrease of translational energy, Q, can be measured directly and thus permits a direct determination of the excitation energy transferred. During the subsequent unimolecular dissociation of the excited ion part of the excess energy E^+ ("nonfixed energy"), *i.e.* the energy not required for overcoming the dissociation threshold, is released as translational energy T[**] (the fragment ions and neutral particles fly apart relative to the original center of gravity of the masses), and this leads to unsharpness in the energy and thus to a broadening of the collision-induced signals[6]. An analogous signal broadening is found in the unimolecular dissociation of metastable ions (MI spectra). Since, however, the excitation energy and thus also the excess energy of the ions dissociating by collision are on average much higher, the signals in the CA spectra are generally broader than those in the MI spectra[6]. The relationship between the quantities Q and T is shown in Figure 1.

2.2. Collision-Induced Dissociation

Three types of information can thus be obtained from a collisional activation spectrum: 1. the relative intensities of the secondary ions; 2. the translational energy T released on dissociation; and 3. the excitation energy transferred, Q. While the intensity ratios and the energy T released in a dissociation (*i.e.* the peak half-width) are suitable for the characterization of an ion structure, determination of the excitation energy by means of the value Q (together with T) provides an insight into the thermochemical properties of an ion. Work in which these three values were systematically investigated will now be briefly reported.

The intensity ratios of collision-induced fragments were studied by *McLafferty et al.*[1c] as a function of various parameters. It was found that when the translational energy (velocity) of the impacting ions increases there is not only an increase in the yield of the collision-induced secondary fragments but also a change in the intensity ratios between these fragments. As an immediate consequence of an increase in the mean transferred energies, the intensity of fragments having higher activation energies increases more than does that of fragments with lower activation energies. A similar increase in fragmentation processes with higher activation energy is found at high pressures of the collision gas; this is explained by the occurrence of multiple collisions. The nature of the collision gas, however, has no influence at all on the intensity ratios[1c] (and also generally none on Q and T[6]), although it does influence the yield of collision-induced fragments: as the size of the atoms or molecules decreases, the cross section and thus the yield increases, so that helium and H_2 are particularly suitable collision gases.

Especially important is the finding that the intensity ratio of the collision-induced secondary fragments from a given primary ion depends to only a very small extent on the excitation energy, *i.e.* on the energy distribution *before* the collision, as is shown by varying the electron energy or by comparing the collisional activation spectra of field-ionized or electron-impact-ionized molecules[1c,9]. Dependence on the excitation

[*] The abbreviation CID (collision-induced dissociation) is used in addition to CA (collisional activation) [3].

[*] This assumption is valid for ions that undergo little or no scattering, *i.e.* those selected by the slit arrangement out of all the colliding ions.

[**] Not only the excess energy but also the activation energy of the reverse reaction, E_R (if present), contributes to the translational energy T released.

energy is found only, if at all, with processes involving the lowest activation energies[1c].

The decrease in translational energy Q caused by energy transfer on collision, as also the energy T released on subsequent dissociation, have been studied in detail by *Cooks et al.* for the case of the aliphatic alcohols[6]. It was established, taking into account the internal energy present before the collision, that the decrease in translational energy Q in a specific collision-induced fragment is equal to the excitation energy predicted from the breakdown diagram, at which the fragment in question is most probably formed. Furthermore, the values of Q and T can be used to obtain information on how the excess energy of a highly excited primary ion will be distributed on decomposition between the translational energy T and/or the excitation energy of secondary fragments and/or the neutral particles ejected (energy partitioning). Finally, for diatomic and triatomic molecules it is possible to derive, from the quantity Q, the *electronic* state in which the collision-induced fragments are formed[5].

2.3. Methods of Measurement

Since the place where collision-induced fragments are formed in the mass spectrometer is the same as for metastable ions (one of the field-free regions of the spectrometer), they can be detected by the same methods. Collision induced fragments can be observed in any mass spectrometer working with a magnetic field[1a, 1b, 2, 3, 5, 6]. However, double-focussing spectrometers with "reversed" Nier-Johnson geometry are particularly suitable for this purpose; in these the ion source is followed first by the magnetic and then by the electric sector[11, 12]. Such an arrangement, as used in principle also in the MIKE[11c] or the DADI technique[12] for the detection of metastable ions, is shown schematically in Figure 2.

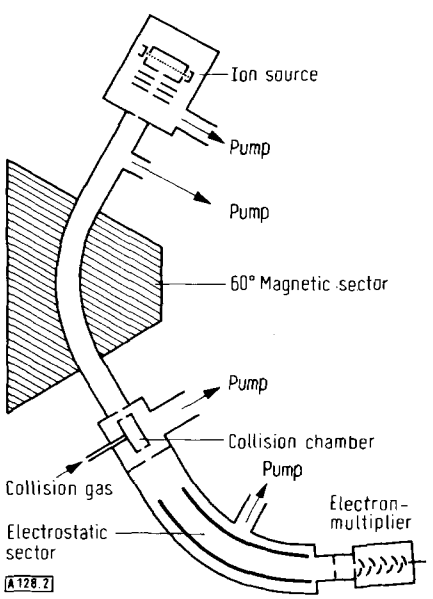


Fig. 2. Schematic layout of a mass spectrometer suitable for the measurement of collisional activation (CA) spectra.

Out of the large number of primary and secondary fragments formed in the ion source the ion to be examined is selected by means of the magnetic field and passes with high translational energy (3—10 keV) into the collision chamber[10]. The collision gas (*e.g.* helium) is admitted through a high-vacuum valve into the collision chamber where the pressure is 10^{-4} to 10^{-5} torr. A differential pumping system prevents all but small amounts of the collision gas from entering the ion source or the electric sector. (To increase the reproducibility in structural studies of organic ions it has proved advantageous not to carry out the investigation at constant pressure but instead at a constant scattering cross section, which is different for ions of different masses.) In a manner analogous to the DADI technique, the collision induced fragments can be subjected to energy and thus mass analysis by scanning of the electrical sector potential.

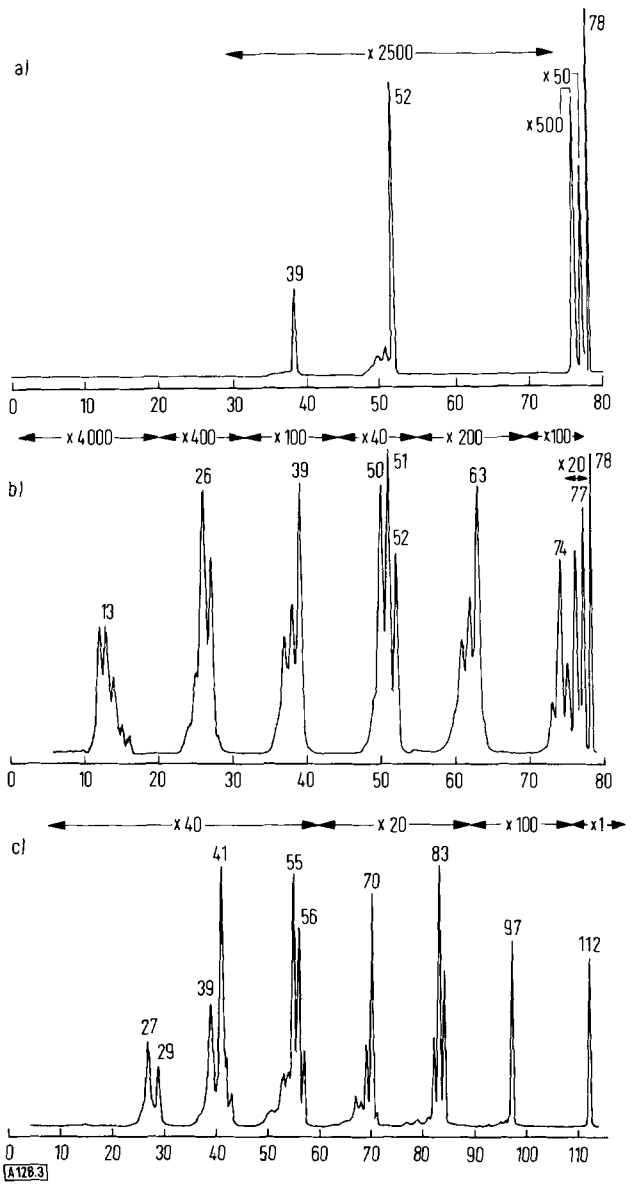


Fig. 3. a) DADI spectrum of the benzene molecular ion ($m/e = 78$); b) CA spectrum of the benzene molecular ion ($m/e = 78$); c) CA spectrum of the 1-octene molecular ion ($m/e = 112$).

Figure 3b shows a collisional activation (CA) spectrum obtained in this way for the benzene molecular ion[*]. In

[*] Strictly speaking, the spectrum in Fig. 3b shows a superposition of collision-induced and unimolecular dissociations, so that a pure CA spectrum is obtained by subtracting the metastable ions corrected for the different scattering cross-sections in Fig. 3a from Fig. 3b. However, this subtraction is not necessary for most analytical purposes.

Figure 3a is shown the same spectrum, but one obtained without a collision gas, *i.e.* a DADI spectrum[12], which contains only the *unimolecular* dissociations of metastable molecular ions. Comparison of Figures 3a and 3b shows that the CA spectrum contains many more signals, more intense but also markedly broader, than there are in the DADI spectrum. The slight shift of the peak maximum in the direction of smaller masses is to be ascribed to the decrease, discussed above, in the translational energy by the amount Q as a result of the collisional excitation. The varying half-widths of the signals, which reflect the translational energy released in the dissociation, are clearly recognizable.

The linear mass scale is an advantage. Nevertheless, the figure also shows at once a considerable drawback of the method. In spite of the relatively small precursor mass of benzene ($m/e=78$) the signals overlap, in some cases to an appreciable extent. Although the resolution is much better with many other compounds because of the smaller amount of energy released in the fragmentation, *e.g.* with 1-octene ($m/e=112$, Fig. 3c), it is rarely possible to resolve individual signals even partially with an accelerating potential of 10 kV and above a precursor mass of $m/e=150$[*]. This does not reduce the method's value for the elucidation of the structure of organic ions, because for this purpose it is only necessary to determine whether two spectra are the same or different. The limited mass resolution does, however, make it considerably more difficult to carry out an isotope-labeling analysis in the case of the larger organic ions. What is favorable, nevertheless, is that only partial incorporation of labeled atoms does not disturb isotope-labeling analyses, since with the above-described magnetic field and electrostatic analyzer arrangement the mass analysis occurs *before* the collision-induced dissociation.

Finally, mention must be made of an interesting variant for the production of collision-induced fragments, described by *Beynon et al.*[13]. In this "surface-induced dissociation" (SID) method the primary ions do not collide with a collision gas but glance a metal surface where collision-induced fragmentation occurs, analogous to that described above[**].

2.4. Characterization of Ion Structures

According to the quasi-equilibrium theory (QET) describing mass-spectrometric dissociation, the intensity ratio of mass-spectrometric fragments depends both on the energy distribution in the primary ion and on the rate constants for dissociation[8]. The rate constants of a given ion are, further, an unequivocal function of the vibrational and rotational frequencies as well as of the activation energies for subsequent dissociations. Ions having the same elementary composition but different structure should thus differ at least partially in their vibrational and rotational frequencies and in the activation energies of the subsequent reactions, and consequently, with the same energy distribution, in the intensity ratio of the subsequent dissociation processes. Since the CA spectra are largely independent of the distribution of excitation energy (see Section 2.1), they reflect the structure of the ion directly. *Thus, if the CA spectra of two ions having the same elementary composition agree both in the intensity ratio and in the peak half-width (translational energy released), then the conclusion is drawn that the structures are identical, and vice versa.* This *comparative* method requires knowledge of the structure of one of the ions. If there is no suitable reference ion, then the structures can in some circumstances be derived from the fragmentation behavior, which in turn can be clarified by isotopic labeling.

If, after the exclusion of the processes with the lowest activation energy[*], the intensity ratio is found to depend on the electron energy, then it can be concluded that a mixture of *non-interconverting* structures is present, the latter being formed simultaneously from the precursor ion by competing mechanisms with different activation energies. Because of the different activation energies the composition of the mixture changes as a function of the excitation energy. On the other hand, if the intensity ratio changes little or not at all with the electron energy it cannot be definitely concluded that only a single structure is involved; *interconverting* structures (isomerization) may be present before the collision, even if the subsequent collision-induced dissociation occurs predominantly through one of them[**].

2.5. Comparison with Other Methods for the Determination of the Structure of Ions in the Gas Phase

The collisional activation technique for the determination of the structure of organic ions competes with several older methods which also differ themselves in the information they provide. If we exclude the very indirect method in which conclusions about the structure of an ion are drawn from the reaction mechanism, the following methods have been used most often[14]:

1. Determination of the heats of formation[15],
2. Investigation of ion-molecule reactions[16],
3. Analysis of dissociation products
   a) intensity ratios in the dissociation of metastable ions (MI)[17].
   b) translational energy T released in the dissociation[18], and
   c) collisional activation spectra[1,2].

All these methods are as a rule comparative, *i.e.* if the heats of formation, the ion-molecule reactions, or the dissociation products are the same for two ions of the same elementary composition, it is concluded that the structures are identical, and *vice versa*. The methods differ in that ions with different excitation energies and different lifetimes are investigated.

In the first two methods those ions are studied whose excitation energy does *not* suffice for dissociation within the mass spectrometric time scale. These ions are therefore described as "stable"[***]. In the determination of the heats of formation

[*] The resolving power for a given precursor ion can be improved by increasing the accelerating potential, since the signal half-width is inversely proportional to the velocity of the primary ion.

[**] Improvements in this technique are currently being studied in many laboratories [20].

[*] Since these processes—recognizable by the presence of intense unimolecular dissociation in the MI spectra—often depend on the energy distribution, any structural assignments based on these peaks, if at all possible, must be made with caution.

[**] In rare cases the absence of an energy-dependence of the CA spectrum may be due to presence of a mixture of non-interconverting structures that happen to have the same kinetic parameters.

[***] "Stability" means that no further decomposition occurs. Of course, isomerization of the ion may perhaps take place.

ions with a minimum of excitation energy are present. (This still depends on the kinetic shift and in particular on the activation energy for the reverse reaction.) In the study of ion molecule reactions at low pressures, *e.g.* by the ion cyclotron resonance technique (ICR)[16] on the average higher excitation energies are involved, reaching up to the lowest dissociation thresholds. In the determination of the structure of ions by analysis of unimolecular decomposition of metastable ions (methods 3a and 3b), however, ions are studied whose energy does suffice for further fragmentation (often also referred to as "unstable" or "reactive" ions). From the quasi-equilibrium theory it can be deduced that these ions are characterized by a well defined excitation energy that is only slightly higher than the lowest dissociation threshold.

The situation with the collisional activation method described here is more complex owing to double excitation. While it is true that most of the ions entering the collision chamber are stable, *i.e.* they have a spectrum of excitation energies that reaches up to the lowest dissociation threshold, the ions that finally undergo collision-induced dissociation are highly excited *reactive* ions. Since with such highly excited ions direct dissociation of the original stable structure is often just as fast (or faster) as an isomerization that is theoretically possible at higher excitation energies, the relative intensities of the collision-induced secondary dissociations reflect to some extent the structure of the stable ions.

Whether the structural information obtained by the above methods differs or not will depend mainly on the isomerization behavior of the ion in question, as may be seen from Figure 4. If the isomerization threshold (E_i) is appreciably higher than the lowest dissociation threshold (E_{oA^+}), then all the methods will yield the same information (Fig. 4a). If, however, $E_i < E_{oA^+}$ (Fig. 4b), it can be shown by means of the metastable characteristic[17] that A^+ and B^+ dissociate *via* the same structure (isomerization), whereas ion cyclotron resonance measurements and heats of formation give different structures for A^+ and B^+. The CA spectra of A^+ and B^+ should also differ, since, although after the collision a considerable amount of isomerization and thus decomposition by way of B^+ can occur, some of the ions A^+ decompose directly. With very low isomerization thresholds (Fig. 4c) it is still possible for different heats of formation to be found for A^+ and B^+. However, in all the other methods most of the ions isomerize already before the fragmentation to a mixture of A^+ and B^+. Moreover, since in CA investigations the energy-richest ions are preferentially excited by collision[19], and since isomerization can also occur after the collision, the CA spectra of A^+ and B^+ differ little if at all[*]. (The collision-induced fragmentation itself occurs both of A^+ and (preferentially) of B^+.) Finally, the intensity ratio of metastable ions will be the same for A^+ and B^+. (Here the dissociation occurs *via* structure B^+.)

Apart from the excitation energies of the ions under study, their lifetimes play a role in the provision of structural information. In most of the methods this lifetime is similar (10^{-7} to 10^{-5} sec); only in ion-molecule reactions in the ICR cell are ions with very much longer lifetimes analyzed (10^{-3} sec).

A discussion of the sources of error in the methods presented here will be of interest. Reliable determination of the heats

[*] Thus, it is not permissible to conclude from identical CA spectra for A^+ and B^+ that there is no isomerization threshold between the two ions. The threshold may only be relatively small ($E_i \ll E_{oA^+}$).

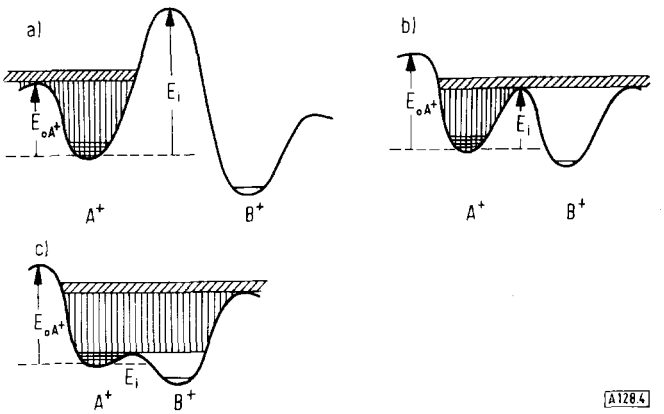


Fig. 4. Influence of internal energy on structural information obtained by different methods about an ion A^+ that may rearrange to an ion B^+ after overcoming an isomerization threshold E_i (the excitation energy region for decomposing metastable ions is hatched diagonally, in CA and ICR investigations vertically, and in measurements of the heats of formation horizontally). a) $E_i \gg E_{oA^+}$; b) $E_i < E_{oA^+}$; c) $E_i \ll E_{oA^+}$.

of formation is often impossible, because the kinetic shift contributing thereto as well as the activation energy for the reverse reaction can generally be obtained experimentally only with difficulty if at all. If the structure of an ion is characterized by means of the intensity ratio of metastable ions (method 3a), the deductions may be false because this intensity ratio depends on the energy distribution. In ion-molecule reactions (ion-cyclotron resonance technique) it is at present not clear to what extent the structure-dependent reactivity of an ion is additionally determined by its excitation energy, the latter being, as discussed above, variable within wide limits.

According to results available so far, the ICR method, CA spectroscopy, and determination of the energy released in the dissociation of metastable ions seem to be the most reliable tools for the determination of ion structures in the gas phase.

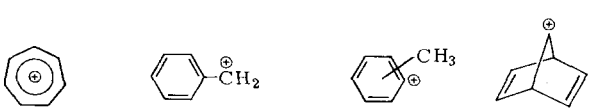
Of these three methods CA is particularly attractive, because a) it is much more sensitive than the other procedures and b) it involves considerably more information (released kinetic energy *and* the intensity ratios of numerous fragments). Its only disadvantage is the poorly defined excitation energy, due to the double excitation.

3. Ion Structures

It was shown in principle in Section 2 when an ion entering the collision chamber will isomerize and what kinetic situation must be present to prevent this process. Examples will now be given for both limiting cases and for transitions between them.

3.1. Carbenium Ions

The classical investigations by *Meyerson et al.*[21] on the structure of gaseous $C_7H_7^{\oplus}$ ions have provoked countless theoretical and experimental studies[*], without it having been

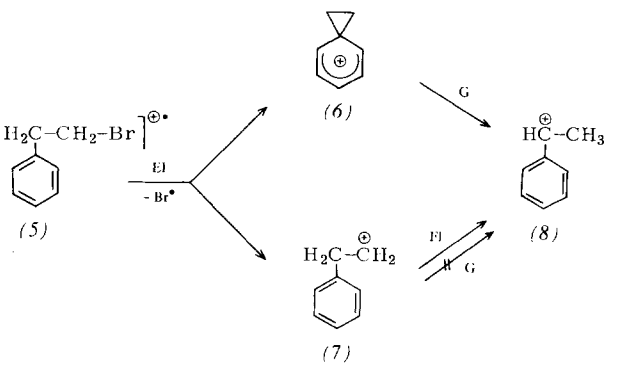


(1) (2) (3) (4)

[*] In this connection particular reference should be made to ICR studies carried out very recently [22].

made conclusively clear in most cases whether the species exists as tropylium ions *(1)* or as benzyl cations *(2)*[23]. The extensive CA investigations by *McLafferty* and *Winkler*[24] on sixty compounds of different structures that yield $C_7H_7^{\oplus}$ on electron impact appear to have closed this chapter of organic mass spectrometry. Contrary to the deductions from the earlier work, it must now be assumed that in most of the compounds investigated, including the $[M-H]^{\oplus}$ ion from cycloheptatriene itself, which was seen as the prototype for *(1)*, an appreciable fraction of stable $C_7H_7^{\oplus}$ ions is present as *(2)*. Furthermore, the above authors showed that, besides these structures, stable *o*-, *m*- and *p*-tolyl cations *(3)*, and even the norbornadienyl cation *(4)*, can be detected when suitable precursors are used. The isomerization threshold between the ions *(1)* to *(4)* appears to be too large for complete equilibration. From the experimental findings it follows further that no $C_7H_7^{\oplus}$ ion possessing only the tropylium structure could be found. Out of all the compounds studied so far the $[M-Cl]^{\oplus}$ ion of (acyclic!) 2,4-heptadien-6-ynyl chloride has the highest proportion of *(1)*, namely >95 %[26][*].

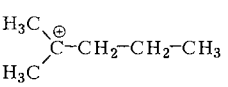
The mutually contradictory results on the structure of gaseous $C_8H_9^{\oplus}$ ions from phenethyl bromide *(5)*[28] could also be largely clarified by CA measurements on deuterated model compounds. Here too a mixture of several species must be present, whose composition was determined by varying the *electron* energy[29]. At the lowest excitation energy (≈11 eV) it contains ethylenebenzenium ions *(6)* as the sole component, whereas in the 70-eV spectra the main proportion consists of 1-phenylethyl cations *(8)*. In the medium-energy region 2-phenethyl cations *(7)* also occur, but, in contrast to the rearrangements of $C_8H_9^{\oplus}$ ions in the condensed phase[30], these do not act in the gas phase as precursors for the ion *(8)* (Scheme 1).



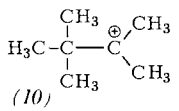
Scheme 1. $C_8H_9^{\oplus}$ ions from phenethyl bromide *(5)*. G = gas phase, Fl = liquid phase, EI = electron-impact ionization.

The problem of the structure of reactive $C_6H_6^{\oplus\cdot}$ radical cations (especially ionized benzene), which has been studied by many groups and by almost every available method, has also recently been clarified by CA measurements[19,31,32]. Investigations of ^{13}C-labeled 1,3-hexadien-5-yne[32] provide, *inter alia*, the first experimental proof that the mechanism previously postulated for the H-scrambling process[23,33] in ionized benzene may proceed reversibly via *acyclic* intermediates (namely 1,3-hexadien-5-yne). It can be further concluded from the CA spectra that hexadiyne radical cations participate only to a minor extent in this equilibrium[31,32], a result that is also in accord with the results of elegant electron impact investigations reported by *Momigny*[34].

In addition to CA investigation of highly unsaturated carbenium ions such as $C_6H_5^{\oplus}$[19,31,35], $C_6H_6^{\oplus\cdot}$[19,31,32], $C_6H_7^{\oplus}$[35], $C_7H_7^{\oplus}$[24,26], $C_7H_8^{\oplus\cdot}$[25,1d], $C_7H_9^{\oplus}$[36], $C_8H_8^{\oplus\cdot}$[31], $C_8H_8^{2\oplus}$[31], $C_8H_9^{\oplus}$[29], and $C_9H_7^{\oplus}$[39] which will not be discussed here, the behavior of more saturated molecular ions and fragment ions on isomerization has also been studied[35,37,38]. To a first approximation, the results obtained so far permit the following generalization: Fragment ions of composition $C_nH_{2n+1}^{\oplus}$ (n=3–7), $C_nH_{2n-1}^{\oplus}$ (n=3–7), and $C_nH_{2n-3}^{\oplus}$ (n=6 or 7) give almost identical CA spectra, independently of the structure of the molecular ions and also independently of the excitation energy, a result that indicates almost complete equilibration of the differently branched ions (Fig. 4c). Although ten molecules having different carbon skeletons were used as precursors, the isomeric $C_6H_{13}^{\oplus}$ ions, for example, decompose largely from one structure, *(9)*, while for $C_7H_{15}^{\oplus}$ decomposition from the structure *(10)* was postulated[37a].



(9)



(10)

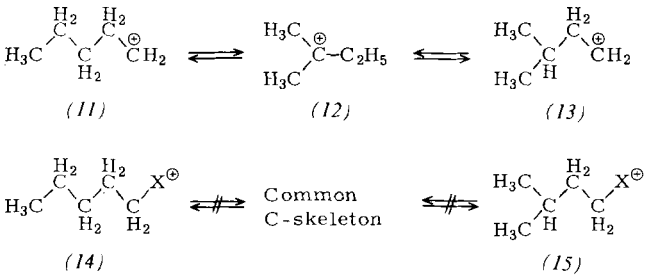
In contrast to this complete isomerization of fragments (even-electron carbenium ions), hardly any isomerization of the carbon skeleton *before* the fragmentation was observed for the molecular ions of isomeric octanes, octenes, cycloalkanes, (except for *n*-propylcyclopentane, which isomerizes to 1-octene before fragmentation), or $C_8H_{14}^{\oplus\cdot}$ radical cations. Hydrogen shifts, however, occur so rapidly that, judged from CA spectra, localization of the double bond, *e.g.* in isomeric octenes, appears so far to be possible only to a very limited extent.

The very different behavior of molecular ions and fragment ions on isomerization appears to be due to the different activation energies E_0 for further decomposition. From measurements of the appearance potentials it can be concluded that the E_0 for further decomposition of fragment ions is generally appreciably greater than the activation energy required for the primary fragmentation of molecular ions. When the relationship between E_0 and kinetic processes, discussed in Section 2.4, is taken into account, this means that for molecular ions $E_i > E_0$ and isomerization is suppressed in favor of fragmentation.

It must be mentioned that this behavior of molecular and fragment ions is not generally valid but that other, still unknown, factors play a part with C_nH_{2n-2} compounds of lower molecular weight[35], with arenes[24,25,31], and with alkynes isomeric with the latter[32,39].

However, the importance of the threshold energy ratio E_i/E_0 for the structural *stability* of the carbon skeleton is shown by a study of isomeric ions containing a heteroatom[40]. Whereas isomeric $C_5H_{11}^{\oplus}$ ions having originally the unbranched skeleton *(11)* or the *iso*-skeleton *(13)* isomerize in 10^{-5} sec to a common structure [probably *(12)*[37,41]], the carbon skeleton hardly isomerizes at all *before* the decomposition if the cation contains a charge-stabilizing group X (Scheme 2).

[*] This result confirms earlier energy measurements and investigations of ^{13}C-labeled acyclic model compounds [27], from which it also follows that a considerable proportion of the $[M-Cl]^{\oplus}$ ions from 2,4-heptadien-6-ynyl chloride must be present as tropylium ions *(1)*.



(11) (12) (13)

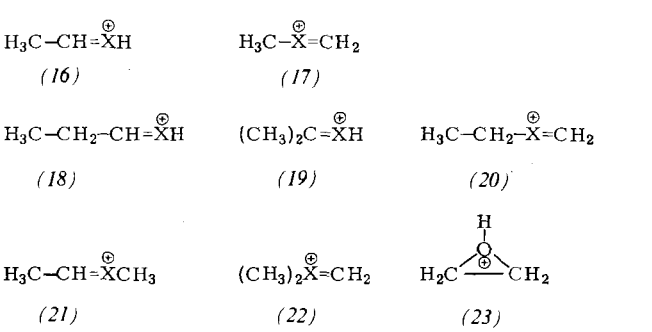
(14) (15)

Scheme 2. Isomerization of carbon skeletons. $X = C{=}O^{\oplus}$, $\overset{\oplus}{O} = CH_2$, $\overset{\oplus}{N}H = CH_2$.

Here too analysis of the energy data shows that the heteroatom group X appreciably increases the potential barrier to isomerization, and this is certainly related to preferential localization of the charge on the heteroatom. The alternative, that the presence of X makes possible other fast reactions that outrun isomerization, probably does not apply here. Similar effects have been found in the CA spectra of immonium ions from oligopeptides containing leucine or isoleucine components. The analytical importance of these differences is discussed in Section 5.

3.2. Oxonium and Immonium Ion

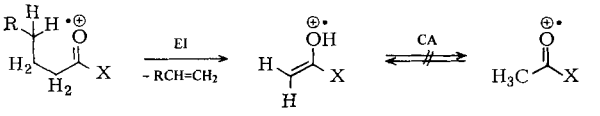
The stabilizing effect of heteroatoms on carbenium centers is well known[*] and is also expressed in the CA spectra of a number of oxonium and immonium ions. In extensive investigations *McLafferty et al.*[1d,43a] detected the structures *(16)*—*(22)* as stable species ($X = O$[1d,43], $X = NH$[43b]). The isomerization thresholds between the ions are so high that rearrangements before or during the collisional activation are almost wholly excluded.



(16) (17) (18) (19) (20) (21) (22) (23)

Since, furthermore, by investigations on numerous precursors it could be shown which structural element of a neutral molecule was to be correlated with which ionic structure, in *unknown* compounds conclusions about the intact molecule could be drawn from the CA spectrum in combination with other mass-spectroscopic data. It is also remarkable that a) a series of structures, *e.g.* protonated epoxides [such as *(23)*], previously considered to be stable, are relatively unstable under CA conditions and rearrange almost quantitatively to *(16)*, $X = O$[1d][**], and b) the CA results are here partly in direct contradiction to interpretations based only on analysis of unimolecular dissociations (including consideration of the kinetic energy released during the dissociation).

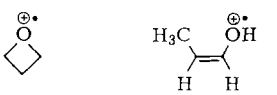
CA investigations of oxygen-containing radical cations of composition $C_2H_4O^{\oplus\bullet}$[46][*], $C_2H_4O_2^{\oplus\bullet}$[48], and $C_3H_6O^{\oplus\bullet}$[49] have also shown that, depending on the primary structure, a series of stable ionic structures exists that are interconvertible with one another only to a limited extent if at all. The structure of ions produced by γ-hydrogen-transfer to carbonyl groups, *e.g.* in *(24)*[50], will be briefly mentioned as an example of non-interconvertible ions. The CA spectra show, in agreement with other methods of investigation, *e.g.* ion cyclotron resonance mass spectrometry, that the energy barrier for interconversion cannot be surmounted (Scheme 3).



(24) (25) (26)

Scheme 3. γ-Hydrogen transfer in radical cations of carbonyl compounds *(24)*, X = H, alkyl, OH.

In principle, several non-interconverting ions can arise whenever the formation of the primary fragment, *e.g.* $C_3H_6O^{\oplus\bullet}$ from $HO(CH_2)_3Y$, Y = Cl, Br, or OH, involves several cyclic transition states sensitively influenced by molecular parameters, *e.g.* bond energies or steric effects, and when isomerization after the fragmentation (*e.g.* elimination of HY) is little favored on energetic grounds. For example, compounds $HO(CH_2)_3Y$ in which Y = Cl, Br, OH afford $C_3H_6O^{\oplus\bullet}$ ions of structures *(27)* and *(28)*, whereas when $Y = OCH_3$ only *(28)* is produced[49].



(27) (28)

Y	(27)	(28)
Cl	60	40
Br	33	67
OH	50	50
OCH_3	0	100

4. Reaction Mechanisms

As has already been mentioned in Section 3, there is a direct correlation between the fragmentation mechanisms and the structures of the ions produced. While labeling studies can provide information on the origin of transferred or eliminated atoms or groups, in the strict sense they contribute little to our knowledge of the structure of the nonreactive species formed. On the contrary, there are many reactions whose mechanism remains obscure in spite of intensive labeling. Here CA spectroscopy with the use of appropriate reference spectra seems to be the method of choice for clarifying the reaction route *via* a determination of the ion structures. In what follows a few examples will be used to show both

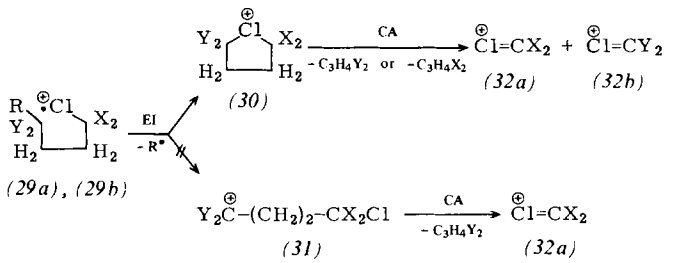
[*] MO calculations show that *e.g.* $CH_2OH^{\oplus}$ and $CH_2NH_2^{\oplus}$ ions are stabilized with respect to $CH_2H^{\oplus}$ ions, by 48 and 66 kcal/mole, respectively [42].

[**] It was recently shown by CA investigations [44] with equipment of considerably improved energy resolution, that ions of structure *(23)* can arise if 2-bromo- or 2-nitroethanol is used as precursor. Also, in the same study [44], the formation of the protonated thiirane *(23)*, S in place of O, was demonstrated, whereas the unbridged $HS{-}CH_2{-}CH_2^{\oplus}$ ion is unstable under CA conditions. SCF-MO calculations [45] lead to the same result.

[*] For $C_2H_4O^{\oplus\bullet}$ ions it could be shown also by analysis of the signal shapes and of the translational energy released in the unimolecular dissociation [47] that, in agreement with CA studies, only a few structures are stable.

the importance and the limitations of collisional activation mass spectrometry in the clarification of such questions.

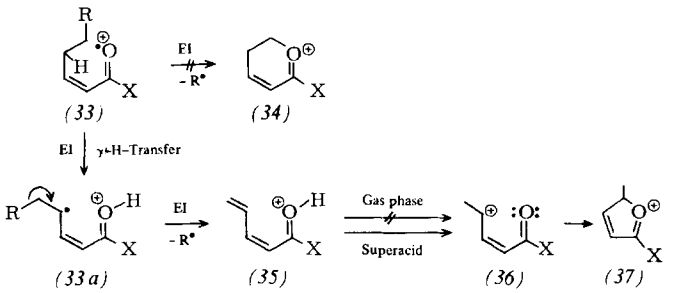
Intense ions of elementary composition $C_4H_8Cl^{\oplus}$ are characteristic for the mass spectra of higher *n*-alkyl chlorides ($n \geq 6$) *(29)*[51]. Although numerous indirect arguments indicated a tetramethylenechloronium ion *(30)* as the structure, direct experimental proof was first achieved by a CA investigation of labeled *n*-alkyl chlorides (Scheme 4)[52]. The finding that *(32a)* and *(32b)* are formed in the same ratio from both precursors *(29a)* and *(29b)* permits only the cyclic structure *(30)* on the grounds of the symmetry properties of *(30)* and *(31)*[*].



(29a), X = H, Y = D; *(29b)*, X = D, Y = H

Scheme 4. Structure of $[M-R]^{\oplus}$ ions obtained from *(29a)* and *(29b)*.

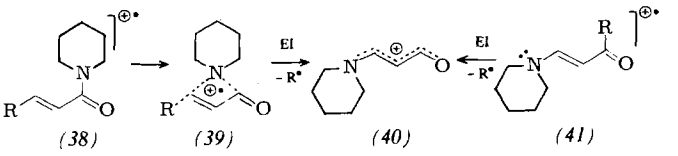
The question of the structure of $[M-Alkyl]^{\oplus}$ fragments from α,β-unsaturated carbonyl compounds (Scheme 5), which received contradictory answers in the literature, could also be decided in favor of the *acyclic* structure *(35)* by CA investigations[53]. Substituted dihydropyrylium ions *(34)*, postulated by *McLafferty*[54], could be excluded with certainty for aldehydes and ketones and with high probability for esters. The course of the reaction is compatible only with a reaction that starts with a γ-hydrogen-transfer and gives the conjugated oxonium ion *(35)* by allylic fission[55]. It is further remarkable that in the gas phase *(35)* does not undergo rearrangement to *(37)*, which *Olah et al.*[56] were able to observe on reaction in a superacid medium.



Scheme 5. Alkyl elimination from radical cations of α,β-unsaturated carbonyl compounds *(33)*, X = H, CH_3, OCH_3; R = alkyl.

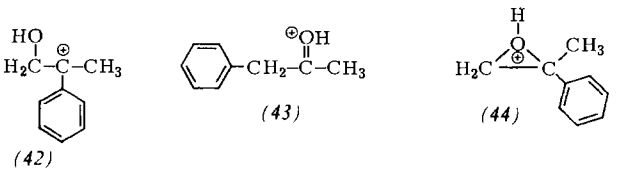
The unusual fragmentation behavior of amides, especially piperidides, of α,β-unsaturated carboxylic acids[57] was also clarified by CA investigations[58]. According to the CA spectra, the $[M-R]^{\oplus}$ ions of *(38)* exist partly as *(40)*; formally speaking the reaction route *(38)* → *(40)* is the first example of an electron-impact-induced intramolecular Michael addition (Scheme 6). The $[M-R]^{\oplus}$ ions from enamino ketones *(41)* serve as reference ions.

[*] It proved possible to exclude complete H/D scrambling [52].

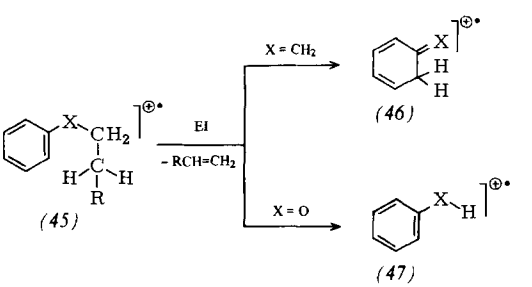


Scheme 6. Radical elimination from radical cations of α,β-unsaturated carboxylic acid piperidides *(38)*, R = alkyl, benzyl, aryl.

Reciprocal[1,2] shifts, which in the limiting case of a concerted course can also be considered as electron-impact-induced dyotropic rearrangements[59], could also be confirmed by CA investigations[60]. For example, the ion *(42)* rearranges completely to *(43)*. The protonated epoxide *(44)* *cannot* be detected under CA conditions.



Much space is devoted in mass-spectrometric literature to hydrogen transfers occurring in alkylarenes with elimination of alkenes, but in many cases it has not been possible to generalize about the transfer mechanism (*e.g.* ring size of the transition state if heteroatoms are incorporated into the side chain) or to clarify the structure of the resulting $[M-Alkene]^{\oplus\bullet}$ ions (Scheme 7). Here again CA spectroscopy provided the answer. Whereas with compounds of the type *(45)*, X = CH_2, the hydrogen transfer takes place exclusively to the benzene ring [formation of *(46)*[25]], ionized phenols *(47)* are formed almost exclusively from alkyl aryl ethers *(45)*, X = O[61][*]. In addition, it could be proved, by a combination of field ionization kinetics (FIK) and CA[61b], that the H-transfer in phenyl *n*-propyl ether (Scheme 7, R = CH_3, X = O) is not preceded by H-scrambling in the side chain, but that the hydrogen is transferred to the oxygen through transition states of various ring sizes; on energetic grounds (lowest activation energy) a transition state with a five-membered ring is favored (transfer of a hydrogen from the methyl group to the oxygen).

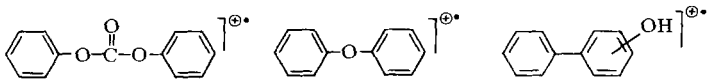


Scheme 7. Alkene elimination with hydrogen transfer from compounds *(45)*, X = CH_2, O; R = H, alkyl.

The question of the structure of the $[M-CO_2]^{\oplus\bullet}$ ions from diphenyl carbonate *(48)*, and thus also of the course of this extrusion reaction, could equally be answered by CA mass spectrometry[63]. In agreement with the results of *Beynon et al.*[64a], the CA results prove that $[M-CO_2]^{\oplus\bullet}$ exists as diphenyl ether *(49)* and not as phenylphenol *(50)*. The differ-

[*] ICR investigations also show that the $[M-Alkene]^{\oplus\bullet}$ ions from alkyl phenyl ethers exist as ionized phenols [62].

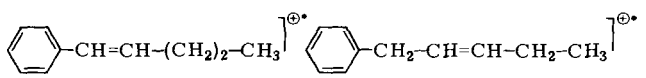
ences observed by *Williams et al.*[64b] in the unimolecular dissociation of the metastable ions from *(49)* and $[M-CO_2]^{\oplus\bullet}$ ions from *(48)* are thus not structure-determined but result from different energy distribution functions that are in principle to be observed when using MI characteristics. It should also be noted here that so far it has not been possible to differentiate and identify position-isomeric arenes by collisional activation mass spectrometry, except for those compounds that show pronounced *ortho* effects in conventional EI spectra: *(49)* and *(50)* give different and interpretable CA spectra, whereas the spectra of *o*-, *m*- and *p*-phenylphenol are identical[63].



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

Finally it should be mentioned that CA spectroscopy in combination with other methods (D-labeling, measurement of appearance potentials, determination of T_{kin}) has contributed substantially to the clarification of the unusual elimination of ammonia from ω-phenylalkylamines *(51)*[65], a reaction that is of interest in connection with Meyerson's concept of "internal solvation of ions in the gas phase"[66a, 66b]. Only *(52)* is formed by elimination of NH_3 from *(51a)*, whereas *(51b)* gives rise to several olefins, including *(53)* and *(54)*, in a complex reaction.

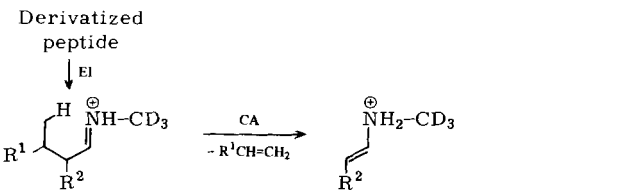
(51a), n = 3 *(52)*
(51b), n = 5



(53) *(54)*

5. Analytical Applications

It is well known that, for example, effective and unequivocal sequence analysis of oligopeptides by mass spectrometry[67] is limited by the following factors: a) the vapor pressure of the sample is too low, b) unspecific pyrolysis reactions occur before the actual electron-impact-induced dissociation and c) the fragmentation behavior of molecular ions and fragment ions is ambiguous, which is a great disadvantage particularly with leucine and isoleucine containing peptides. Whereas the first two effects can be considerably mitigated by use of field desorption mass spectrometry (FD-MS)[68], the limitation due to c) can be reduced by CA spectroscopy: the *structural stability* of the *immonium ions* and the characteristically different CA spectra (see also Section 3.2) serve as a basis for the sequence determination in a peptide. Thus, the CA spectrum of the ion *(55)* shows an intense fragment *(56)* at $m/e=61$ when the peptide derivative contains leucine, whereas if isoleucine is present the fragment *(57)* with $m/e=75$ is formed (Scheme 8)[69]. In the authors' opinion[69], on the basis of the characteristic differences in the CA spectra of other fragment ions, and of the fact that an unequivocal correlation is possible between the CA spectra of non-interconvertible ions and the intact structure of the neutral molecules, even mixtures of oligopeptides can be analyzed.



(55) *(56)*, *m/e* = 61 (R^2 = H)
(57), *m/e* = 75 (R^2 = CH_3)

Scheme 8. Decomposition of immonium ions *(55)* from leucine ($R^1=CH_3$, $R^2=H$) and isoleucine ($R^1=H$, $R^2=CH_3$) fragments.

A completely new procedure for qualitative analysis of mixtures without their previous separation (*e.g.* by gas chromatography) has been proposed by *Levsen* and *Schulten*[70]. These authors pyrolyzed a deoxyribonucleic acid, ionized the pyrolyzate with low electron energy (suppression of fragmentation), and then measured the CA spectra of some selected ions. By comparison with reference spectra they were able to identify, as pyrolysis products *e.g.* methanol, acetonitrile, propargyl alcohol, furan, 2-methylfuran, furfuryl alcohol and α-angelica lactone.

Electron impact in conjunction with collisional activation has also been used by *Kruger et al.*[72] for quantitative mixture analysis. The authors claim that mixture analysis is possible with an accuracy of ±5% if an internal standard is used and report a detection limit of 10^{-10} g.

Because of the multiplicity of fragmentations induced by collisional activation and the fact that the dissociation reactions can be connected with the structure of the reactive species, the CA method should supplement the information from all mass-spectroscopic methods that produce exclusively molecular or quasimolecular ions. The first encouraging works in this direction shows that in combination with, *e.g.* field ionization[9], electron-attachment mass spectrometry[71] (investigation of *negative* ions), or chemical ionization[1d, 44] it is possible to draw conclusions from fragmentation processes about the structure of molecular ions that are stable under the conditions of the ionization method, a feature that was hardly ever possible from FD, FI, EA, or CI spectra alone.

6. Critical Assessment and Prospects

In spite of the undisputed success of mass spectrometry in the elucidation of the structure of organic *compounds*, it is seldom possible by mass spectrometry alone to determine unequivocally the structure of the *ions* formed, and then only—if at all—with the aid of additional techniques. The collisional activation method reviewed here constitutes a very promising supplement to present-day techniques for structure determinations of ions in the gas phase. According to investigations already at hand, the method is reliable, the experimental technique is simple, and the data are easy to interpret. The method shares with most other techniques the disadvantage of being *comparative*. In the absence of suitable reference structures recourse must therefore be taken to additional information, *e.g.* fragmentation behavior, isotopic labeling, and measurement of the appearance potentials; in this connection, com-

bination of CA measurements with isotopic labeling is of special importance.

Although at first the center of interest in CA investigations lay in the structure of organic ions, it may be expected that in future the method will be used more frequently to study reaction mechanisms by clarification of the ion structures. Although the great value of the method for solution of the two problems (ion structures and reaction mechanisms) can hardly be disputed, only the future will show whether the analytical possibilities indicated above are of practical importance; for example, in view of the combination of gas chromatography with mass spectrometry, so widespread today, the direct analysis of mixtures using the CA method will be limited to special problems.

Finally, consider the instrumental side of the method. What is particularly important to note is that all the conventional magnetic instruments can be used for the measurement of CA spectra, which is not the case with the ICR technique. Instruments with the reverse Nier-Johnson configuration are undoubtedly particularly advantageous. Collisional activation mass spectrometry has a higher sensitivity than the competing techniques (ICR and MI), but its limited resolution is a disadvantage. A decisive improvement in resolution was achieved by most groups in 1975 by increasing the acceleration potential to 10 kV. A further doubling of the acceleration potential is conceivable and desirable. A possible alternative to instruments with the reverse configuration is offered by the "linked scan"[20a, 20b], by means of which collisional activation studies can also in principle be carried out with double-focussing instruments of conventional geometry. Only the kinetic energy released in a dissociation cannot be measured by this method.

The spread of a new analytical method depends further, and decisively, on the commercial availability of the necessary instrument. Mass spectrometers with additional equipment for the determination of CA spectra have recently been offered by two companies, so that it may be expected that collisional activation studies will in future be carried out routinely in organic mass spectrometry for the determination of ion structures and reaction mechanisms.

The authors should like to extend their sincere gratitude to Professor F. W. McLafferty, Cornell University (USA), who recognized and systematically studied the potential of collisional activation mass spectrometry for the determination of the structure of organic ions, for his cooperation and for the stimulating influence of his work.

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Predictive Molecular Orbital Calculations in Organic Chemistry

By Joseph J. Dannenberg[*]

The utility and importance of predictive, rather than correlative, molecular orbital calculations in organic chemistry are discussed. Examples of the predictive approach to organic synthesis and the study of organic reaction mechanisms are presented.

1. Introduction

A cursory survey of the chemical literature will very quickly demonstrate the increasing proportion dealing with theoretical treatments of Organic Chemistry. The majority of articles dealing with this subject can be properly described as theoretical explanations or rationalizations of known experimental results. This type of work generally takes one of two forms: either an article devoted to the explanation (often with great insight) of certain reactions or categories of reactions, or what often amounts to a theoretical section, added to an experimental paper, which purports to rationalize the results in an acceptable manner. The latter type of discussion is necessarily less detailed, in general, than the former, as it is rarely the unifying force of the article. The increasing acceptance of these theoretical organic studies testifies to the fact that increasing numbers of organic chemists are coming to accept molecular orbital theory as a part of their scientific world and as a useful contribution to organic chemistry, in particular. Thus, molecular orbital calculations are now generally accepted by most organic chemists as being correlative with experimental results. Nevertheless, many organic chemists continue to ask a very reasonable question which can be stated as follows: "How much do we really benefit from calculations that simply tell us that what we have already experimentally demonstrated is correct?"

Implied in this question is the underlying suspicion that the theoretician might not have arrived at the correct result had he not known it at the outset. An example is shown in Figure 1 which is the representation of a lecture slide[1]

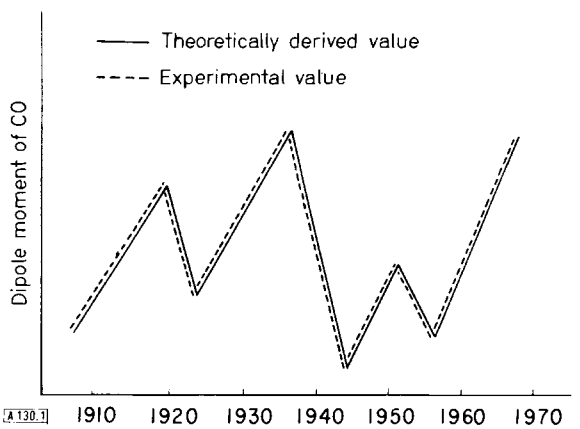

Fig. 1. The experimental and theoretically acceptable values for the dipole moment of carbon monoxide *vs.* time.

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belonging to Professor *Turro* which shows the theoretical and experimentally acceptable values of the dipole moment plotted as a function of time.

In the context of the above discussion, we might reasonably pose the following question: "How can molecular orbital theory be more useful to organic chemistry?" The purpose of this review is to demonstrate that at least one viable answer to this question lies in using molecular orbital calculations to help solve the kinds of problems to which organic chemistry is addressed: Synthesis, mechanistic studies, and structure elucidation. Implicit in the suggestion that molecular orbital calculations be used to help solve problems is the idea that these calculations are to be used not only to explain and interpret results, but also to obtain results by suggesting paths of experimentation. In other words, now that we have confidence in the correlative values of molecular orbital theory, it is time that we used it more as a predictive method. This review will illustrate how molecular orbital calculations on individual systems can be used predictively by experimental organic chemists. Its scope shall be limited to the application of predictive MO theory to organic synthesis and reaction mechanisms. We shall not consider structural elucidation of intermediates since the predictive aspects of such calculations are evident and they have already been discussed in the literature to great extent[2]. Photochemical reactivity is also not discussed *per se*, nor are predictions made by rules such as the Woodward-Hoffmann rules, or those recently proposed by *Salem* for photochemical reactions, both due to space limitation and the fact that they are adequately discussed elsewere[3–5]. All the cases discussed will be concerned with calculations that were explicitly predictive in nature.

2. Methods

Many different methods of doing molecular orbital calculations are currently available. These range from simple Hückel theory to large basis set *ab initio* calculations with configuration interaction (CI). The chemist is confronted with the necessity of making a choice among these. The literature contains many articles extolling the virtues or exposing the detriments of one method or other[6]. We take the view, here, that the choice of the method is generally less important for predictive than for correlative calculations. The various MO methods generally agree with each other much more than they disagree. Since predictions must ultimately be supported by experiment, the burden of proof for the ultimate solution of the problem in question will be largely experimental, not theoretical. Thus, it is advisable to choose a method that is easily accessible and not too costly. Methods such as extended Hückel[7], CNDO[8], INDO[9], MINDO[10] and STO3G[11] generally come to mind as logical choices. Each of these has its own advantages and shortcomings (which shall not be discussed here), yet each is probably within the range of quality/cost that would be acceptable to an organic chemist. Obviously, large scale *ab initio* calculations on most systems of current interest to organic chemists would be prohibitively expensive, both in terms of computer time and experienced manpower.

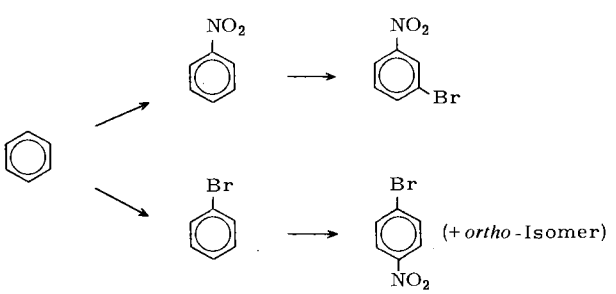
The organic chemist must realize that the results of a molecular orbital calculation at any of the readily accessible levels will not contain the absolute, final word about the system in question. All of the common molecular orbital methods (including the so-called *ab initio* methods[12]) are intrinsically approximative. They are all, therefore, likely to be in error in at least some details. An important criterion for the chemist should be: Do we have sufficient confidence in the prediction of a certain calculation to base an experiment upon its results? If the answer is negative, then one can do more sophisticated calculations until the criterion is met. Exactly what confidence level is acceptable will depend upon the problem at hand. Thus, a prediction that requires a very simple experiment for verification would require a relatively low level of confidence to be acceptable. It may be more costly to increase the confidence level by doing a more detailed calculation than it would be to simply verify the prediction experimentally. This argument becomes more convincing when you remember the result of the more detailed calculation must also be confirmed experimentally. On the other hand, if the experimental verification is costly and time consuming, it might be wise to invest in a more sophisticated calculation before one embarks on what may turn out to be a useless experiment.

It is generally useful to work with readily available programs of established methods, not only because of convenience, but also because there will generally exist a reasonable literature of results using such methods. The results of a particular calculation can often be better interpreted in the context of these results, especially when the limitations of a particular method are of concern.

Finally we must remember that the geometry of the system in question is always part of the input of any MO calculation. The results obtained will be no better than the geometry or geometries used. It is completely absurd to do a very sophisticated and costly calculation on a geometry in which we have little confidence. Part of choosing an appropriate method often includes a means of geometrical optimization of various species and/or reaction paths.

3. Synthesis

All synthetic reactions can be considered in terms of their energy surfaces. Thus, in the simple case of the synthesis of *para*-bromonitrobenzene from benzene, we must first brominate, then nitrate. This can be demonstrated with the aid of a reaction surface such as that of Figure 2. Initial nitration of benzene leads to a point on the surface (nitrobenzene) from which *para*-bromonitrobenzene is inaccessible because



the *col* leading to *meta*-bromonitrobenzene is significantly lower than that leading to the *para* (or *ortho*) product. On the other hand, initial bromination leads to a point on the

surface (bromobenzene) from which *para*-bromonitrobenzene is more accessible. Inspection of this surface would lead the synthetic chemist to choose to brominate then nitrate rather than *vice versa*. Of course, organic chemists know enough about electrophilic aromatic substitution so they do not need to calculate, or even to imagine such a surface in order to choose the correct reaction sequence. There are, nevertheless, cases where consideration of the details of the surface can be extremely useful.

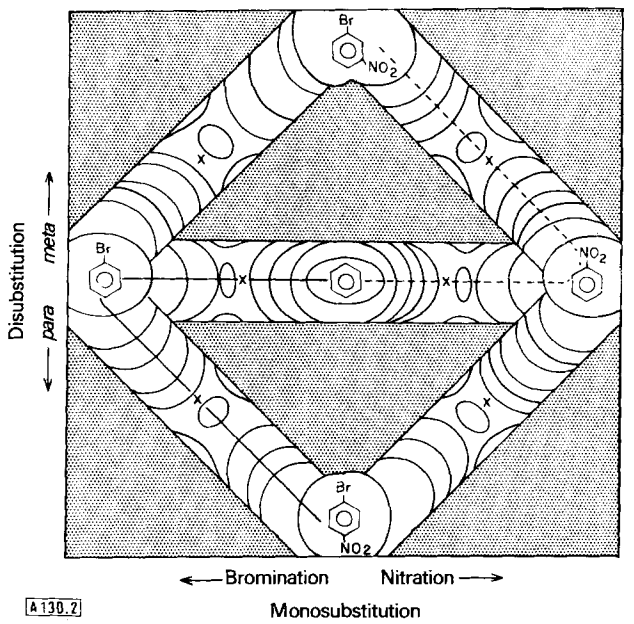
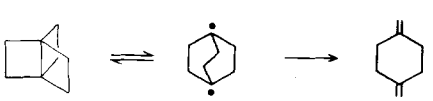


Fig. 2. A composite surface representation of the synthesis of *para*-bromonitrobenzene. The transition state for each step is marked with an "X". The solid line (——) represents the best path toward the desired product, while the dashed line (– – –) represents the best path toward the unwanted *meta* isomer. The surfaces involving *ortho* substitution have been omitted for the sake of clarity.

One such case is the synthesis of [2.2.2]propellane. This elusive molecule confounded the synthetic attempts of several research groups for some time[13]. Frequently, attempts to synthesize [2.2.2]propellane or its derivatives led to the production of 1,4-dimethylenecyclohexane or its derivatives. The reason for this became clear when *Hoffmann* and *Stohrer* showed that [2.2.2]propellane was a case of a species in which two different ground states are possible: one with a bond between the bridgehead carbons and one with a radical site at each of these carbons[14]. These were interconverted *via* a transition state in which the HOMO and LUMO crossed in energy. In other words, the HOMO of *(1)* becomes the LUMO of *(2)*.



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

Both *Hoffmann* and *Stohrer*[14], and later *Newton* and *Schulman*[15] in a more refined calculation, predicted the two species to be of similar energy and the interconversion barrier to be small. As *(2)* is readily expected to immediately rearrange to *(3)* since it is an appropriate model for a transition state of the degenerate Cope rearrangement of *(3)*[16], we are no longer surprised to find *(3)* as the ultimate product of an attempted synthesis of *(1)*. The diene *(3)* can arise either from a successful synthesis of *(1)* which decomposes under the conditions of reaction, or from an unsuccessful synthesis of *(1)* where the region of the surface corresponding to *(2)* is attained and this produces *(3)*, rather than *(1)*. The surface tells us that we must avoid attaining the 1,4-diradical structure if our synthesis is to succeed.

One way of attaining the minimum corresponding to *(1)* without passing through the region corresponding to *(2)* was suggested by simple INDO calculations on both the ground and the first triplet states of the system[17]. This calculation predicted the distance between the bridgehead carbons in the triplet state to be intermediate between those of *(1)* and *(2)*. It also suggested that the ground state geometry that corresponds to the optimized triplet lies on the [2.2.2]propellane side of the barrier between *(1)* and *(2)*. Vertical relaxation of the triplet might then provide an accessible pathway to *(1)* that completely avoids *(2)*. The obvious experiment to do based on these calculations was to excite *(3)* to its triplet state which would undoubtably rearrange to the relaxed triplet *(4)*, since the triplet state of an isolated double bond should be much higher in energy. The reaction must be performed at low temperature because the Newton-Schulman surface predicts that *(1)* should have a half-life of only about ½ hour at room temperature[15]. This prediction is in good agreement with the observed[18] half-life for the decomposition of the *N*,*N*-dimethylcarboxamide derivative.

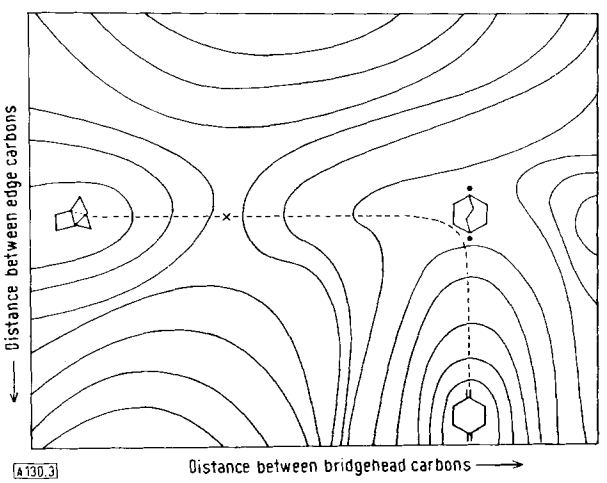


Fig. 3. A possible potential surface for the conversion of [2.2.2]propellane into 1,4-dimethylenecyclohexane. (Fig. 4 represents a horizontal slice through the surface.) The dashed line represents the reaction coordinate. The degenerate Cope rearrangement of 1,4-dimethylenecyclohexane can be understood using this surface by following the reaction path as far as the diradical, then proceeding in another dimension (not plotted) to a degenerate representation of the diene.

The confidence level of this surface (Fig. 4) is not extraordinarily high, due to the propensity of such methods as CNDO and INDO to overestimate the relative stability of small rings[19]. Thus, the ground state surface in Figure 3 is artificially skewed in favor of *(1)*, which may have introduced an error in the calculated position of the *col* between *(1)* and *(2)*. Nevertheless, the extreme simplicity of the suggested experiment (irradiation of 1,4-dimethylenecyclohexane with a suitable triplet sensitizer, at low temperature) made experimentation, rather than a more sophisticated calculation of the triplet

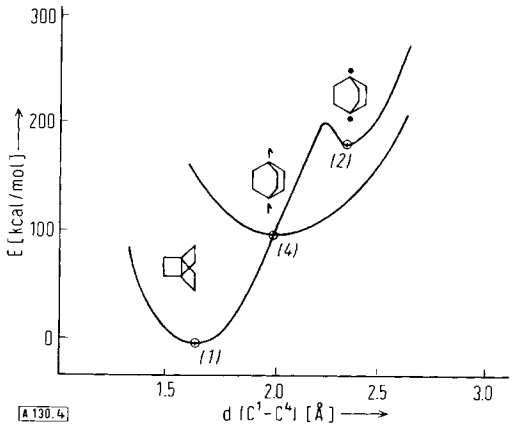
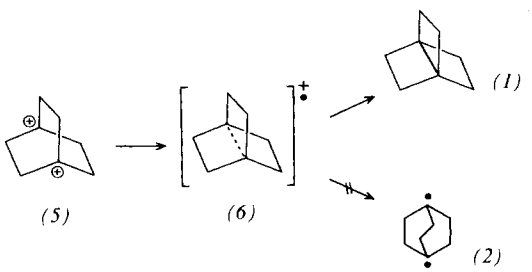


Fig. 4. Plot of energy *vs.* central bond length for the lowest singlet and triplet state of [2.2.2]propellane. Circled points represent optimized geometries. Other bond lengths vary slightly [17].

surface, the logical sequel. The fact that [2.2.2]propellane was indeed synthesized by the suggested method[20] indicates that the INDO surfaces were quite useful despite their approximate character. It is doubtful that a more exact surface would have led to a more fruitful experiment.

Another approach to the synthesis of [2.2.2]propellane[21] can be derived starting from consideration of the 1,4-dication of bicyclo[2.2.2]octane *(5)*. NMR spectra[22], as well various kinds of calculations[22,23], are in accord with a structure for *(5)* having a relatively short distance between the bridgehead carbons.

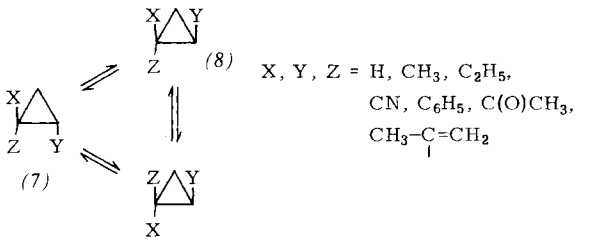


The dication *(5)* is formally equivalent to the dication of [2.2.2]propellane [obtained by removing two electrons from *(1)*]. INDO calculations predict that the stepwise addition of two electrons (reduction) to *(5)* will conserve the short distance between the bridgehead carbons, leading to formation of *(1)* rather than *(2)*. The fact that *(5)* has been prepared only in magic acid[22] whereas *(1)* is expected to be very labile to acid poses a difficult impediment to the realization of a synthesis of *(1)* based on this reaction. If this impediment can be surmounted, the reaction may prove to be the basis of a synthesis of *(1)* in good yield.

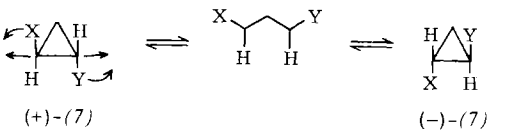
4. Mechanistic Studies

4.1. Cyclopropane Rearrangement

The thermal isomerization of cyclopropane, and particularly the behavior of the presumed trimethylene intermediate, has received considerable theoretical attention during the past several years. Theoretical studies of quite varied levels of sophistication (from extended Hückel calculations with a geometry search in three dimensions[24] to a small basis set SCF *ab initio* calculation in which all 21 internal coordinates were considered[25]) have been reported. These calculations have provoked a number of extremely interesting experimental studies on various model compounds *(7)*[26–29].



On the basis of his extended Hückel calculations with three geometric variables (CCC angle and the torsional angles about each of the two C—C bonds), *Hoffmann* was the first to suggest that there be a relative minimum (or intermediate) on the trimethylene surface that corresponds to a species with all its atoms in the same plane except for the two hydrogens on the central carbon, and a CCC angle of 125°[24]. He further suggested that cyclopropane be preferentially formed from this intermediate by a conrotatory process[24]. The implication of this result is that there ought to exist a low energy path that would convert a molecule of an optically active disubstituted cyclopropane into its enantiomer without the intermediacy of the *cis* isomer.



A few years after *Hoffmann*'s calculation, *Salem et al.* published a detailed surface for trimethylene that specifically considered all 21 internal coordinates[25]. The energies were calculated using a small basis set *ab initio* method that included 2×2 and 3×3 configuration interaction, where important. *Salem*'s surface confirmed *Hoffmann*'s more qualitative observations, while providing much more detail and invaluable insight into the molecular motions involved in the various stages of the reaction[30]. For the first time one could imagine a complete organic chemical reactive process, rather than merely the transition states and/or intermediates. Despite the fact that these and other calculations[31,32] all predicted that the concerted two bond rotation (inversion of *(7)*) should compete favorably with the one bond rotation (*trans*→*cis* isomerization), thermolysis of several appropriately substituted cyclopropanes provided no experimental support for this hypothesis. Confidence in the theoretical predictions eventually led *Berson et al.* to study the thermolyses of *trans*-1,2-dideuteriocyclopropane[33] and *trans*-2-deuteriophenylcyclopropane[34]. Both compounds of type *(7)* exhibit the anticipated double rotation (inversion) process. Apparently, the more drastic substitutions used by previous workers[26–29] were sufficient to cause a significant change in the potential surface. A recent report by *Simonetta et al.* shows that even calculations so simple as extended Hückel account for the difference in reactivities between cyclopropane and various derivatives[35]. An important point to emphasize here is that simple calculations on actual experimental systems are often indicated, even in the presence of extremely sophisticated analyses of model systems.

4.2. Nucleophilic Substitution

The mechanism of nucleophilic substitutions, particularly solvolyses, continues to be an area of considerable interest and importance to organic chemists. Various experimental advances have allowed us to progress from the classical S_N1 and S_N2 ideas of *Ingold*[36], through the kinetically determined intermediates referred to as "intimate" and "solvent-separated ion pairs" by *Winstein*[37], to several additional refinements including "solvent-assistance"[38] and the suggestion that the "S_N2" reaction occur *via* the intermediacy of an "intimate ion pair"[39]. Several mechanistic schemes based upon various distillations of experimental results have recently appeared[39–41]. Theoretical work had been limited to S_N2 reactions, usually the reaction: $F^- + CH_3F \rightarrow CH_3F + F^-$[42, 43]. While reactions of this type are of real interest, particularly in the context of the increasing power of molecular beam techniques, they are only distantly related to the equivalent reactions in solution. Therefore, they are not directly applicable to the design of a solvolysis reaction. We have recently completed an INDO study of the substitution of water upon protonated alcohols[44].

$$H_2O + ROH_2^+ \longrightarrow H_2OR^+ + OH_2$$
$$R = CH_3,\ C_2H_5,\ CH(CH_3)_2$$

The predicted lowest energy reaction paths were calculated by performing extensive geometrical optimization at many points along the reaction coordinate. Analysis of the reaction paths led to the suggestion that the intermediates observed by *Winstein et al.* might better be described as anion-stabilized intermediates (ASI) and anion-cation stabilized intermediates (ACSI) rather than "intimate" and "solvent-separated ion pairs". These intermediates, particularly the ACSI, can be conceived with *defined structures* that allow for experimental verification (see Fig. 5). In addition, once the natures of the intermediates have been theoretically approximated, it

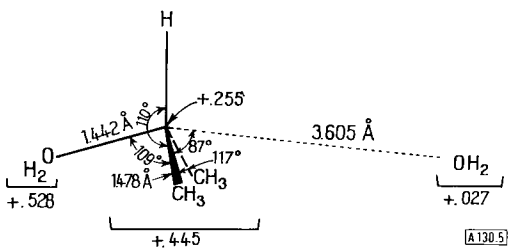
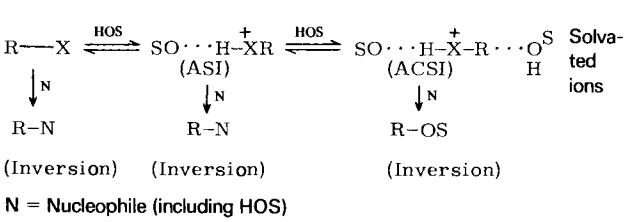


Fig. 5. The calculated geometry for the anion-cation stabilized intermediate (ACSI) for reaction of water with protonated isopropanol.

becomes possible to imagine various categories of nucleophilic substitution that can be defined in terms of the anion-stabilizing, cation-stabilizing and general ionic solvating properties of the medium. Thus, it is possible to accommodate many seemingly divergent experimental results using these ideas.



Perhaps the greatest didactic advantage of generating a purely theoretical reaction mechanism is that a continuous, self-consistent picture is generated. Such a formulation can provide a very useful comparison to reaction mechanisms generated from experimental results. The latter are generally analogous to curves generated by extrapolation between points. Since various experiments which are related or extrapolated to the same mechanism are often performed under different conditions, the extrapolation is often necessarily made between points on slightly different reaction surfaces. For example, the measurement of a rate constant provides information about the energy, but not the geometry, of a transition state. A spectrum of a cationic intermediate stabilized in magic acid provides structural information and often some energetic information, about an intermediate, but generally on a reaction surface that may be significantly different from that relating to the rate constant.

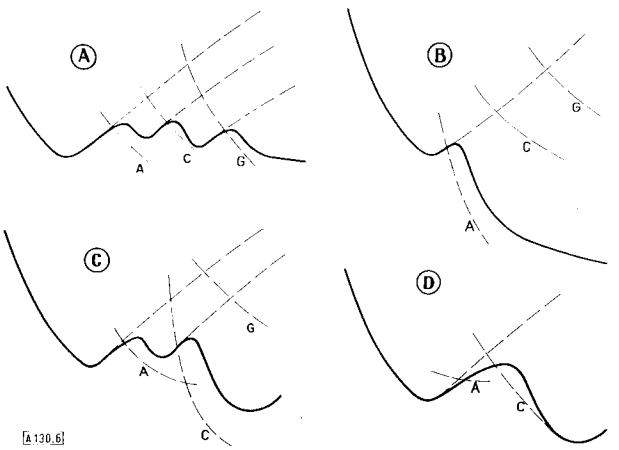


Fig. 6. Energy (vertical) *vs.* reaction path (horizontal) diagrams for various possible types of nucleophilic substitution obtained by adding anion stabilization (A), cation stabilization (C), and general solvation (G) to an arbitrary reaction coordinate for heterolytic R—X bond cleavage. Broken lines indicate individual contributions while the solid line indicates the sum in each case. Ⓐ, anion- and cation-stabilization are sufficiently balanced to allow two intermediates (ASI and ACSI) between reactants and solvated ions. Ⓑ, the solvent is such a strong anion stabilizer (*e.g.* magic acid) that the R—X bond breaks directly into solvated ions. Ⓒ, a moderate anion-stabilizing solvent plus a strong cation-stabilizer (which may be an added nucleophile, *e.g.*, azide) leads to formation of product directly from the first intermediate (ASI). Ⓓ, a poor anion-stabilizing solvent (*i.e.* aprotic) and a strong cation-stabilizer (*i.e.* nucleophile) lead to product by direct attack on the reactant (classical S_N2).

Once an approximate energy surface or reaction path has been calculated, it may become possible to define critical experiments to test the surface at various points. If the results of these experiments are in accord with the predicted reaction path, one can, in general, gain confidence in the entire reaction path (of course, you would have to test the reaction path at an infinity of points to have complete confidence). There is a great conceptual value in such a procedure. An analogy is depicted in Figure 7 in which one tries to determine the best path through a forest. Experiments might show the absence or presence of trees at the points indicated. There are several reasonable ways to connect the unobstructed points in a path. In addition, it is not necessary that all the points must lie on the path. In Figure 7, the location of the path is predicted by theory. Experiments can be performed to determine the presence or absence of obstructions at various points along the predicted path. The presence of such an obstruction would indicate an erroneous prediction. The absence of

obstructions along several properly spaced points along the path would increase confidence in the prediction even if there were shown to be points off the path where obstructions were also absent.

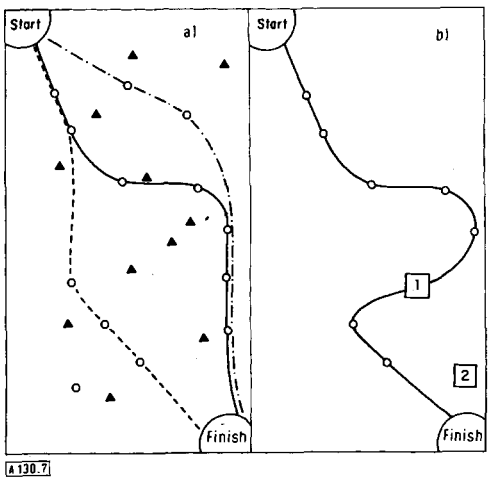
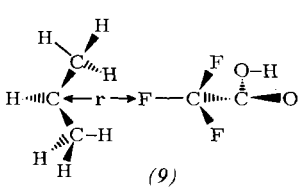
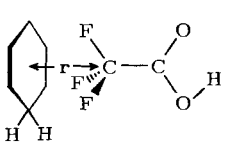


Fig. 7. a) An experimental attempt to find the path (we assume only one exists) through a forest from "start" to "finish". Points marked ▲ represent experimentally determined obstacles (*e.g.* trees); points marked o represent experimentally determined clear areas. There are several reasonable formulations of the path based on these data (——, – – –, ·—·) yet no *a priori* means of choosing among them.
b) A theoretically predicted path through the forest (——) fits many experimental clear areas and encounters no obstacles; yet it is different from the three most obvious paths (cf. a)). Experiments at points 1 and 2 are indicated. A clear area at 1 and (to a lesser extent) an obstacle at 2 would greatly increase our confidence in the prediction.

The calculation of the true energy surface (or reaction path) for a solvolysis reaction would necessarily take into account more geometric variables than is generally practicable: the internal coordinates of the reagents plus a sufficiently large number of solvent molecules[45]. Nevertheless, the organic chemist often knows enough to make a wise choice of a simplified model. Thus $H_2O+ROH_2^+$ is probably a better model for a solvolysis than is F^-+RF since the differential effects of solvation during the course of the reaction should certainly be smaller in the former case.



(9)



(10)

The specific effects of solvents can also sometimes be treated in a predictive manner using molecular orbital theory. Thus, the seemingly anomalous behavior of trifluoroacetic acid (TFA) as a cation solvent has been explained by the suggestion that the trifluoromethyl group might interact with cations in a stabilizing, yet non-nucleophilic (*i.e.* non bond-forming) manner[46]. The prediction of *(9)* as a model for a 2-propyl cation-TFA interaction, and *(10)* as a model for a protonated benzene-TFA interaction should be testable by suitable experiments, some of which are currently being undertaken in our laboratories[47].

5. Conclusion

The predictive powers of even relatively simple molecular orbital calculations can be used to provide the organic chemist with a powerful new tool to help devise experiments and mechanistic theories. This tool can be easily used by organic chemists as the molecular orbital procedures are neither costly nor difficult. The organic chemist can best tailor the calculations to the problem at hand when he performs them himself. He is also best equipped to determine what experiments are likely to be both practical and critical tests of the theoretical predictions. The types of predictive theoretical studies discussed in this review should be treated as approaches, rather than solutions to problems in organic chemistry. An acceptable solution almost always will require experimental verification.

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Radioimmunoassay

By Hans Georg Eckert[*]

Biologically active substances are often effective in nanogram or even smaller quantities. Investigations of their mode of action therefore require highly sensitive microanalytical methods of detection. Chemical, chromatographic or spectrometric methods frequently lack the required sensitivity; it was only after the discovery of the radioimmunoassay (RIA) that quantitative determination of minute amounts of substances in the presence of a millionfold excess of other compounds became possible. The radioimmunoassay combines the extreme sensitivity of detection of radioactively labeled substances with the high specificity of immunological reactions. The superiority of radioimmunological methods over other analytical techniques rests upon their sensitivity, specificity, facile application, and especially their broad general scope.

1. Introduction

The first results suggesting the feasibility of the radioimmunological method were obtained in studies performed by *Yalow* and *Berson*[1] in the 1950's. During *in vivo* studies on the metabolism of [^{131}I]-insulin they surprisingly discovered that all diabetics having undergone insulin treatment had formed insulin-binding antibodies. Further studies showed that (i) an excess of insulin saturates the antibody-binding sites and (ii) addition of non-labeled insulin displaces radioactively-labeled [^{131}I]-insulin from the gamma-globulin complex. Thus the foundation was laid for the development of radioimmunoassay.

Further development of this microanalytical *in vitro* technique then led to the first radioimmunoassay for insulin[2, 3], in which an insulin-specific antibody was the key reagent. Almost simultaneously, *Ekins*[4] reported a very similar principle for determining the thyroid hormone thyroxine (T4). However, instead of an antibody, a naturally occurring transport protein, *i.e.* thyroxine-binding globulin (TBG), served as specific binding reagent. On the basis of these studies, numerous radioimmunoassays have since been developed for a wide variety of substances, and variations in the technique have led to a series of similar methods described in numerous books and reviews[5–11], and variously known as saturation analysis, radioligand assay, and competitive protein binding analysis.

The far-reaching significance of and the great interest in these sensitive methods of determination are apparent from the handsome number of over 200 radioimmunoassays available to date. Using these methods, various substances can be determined in nanogram to picogram, and sometimes even smaller amounts without previous separation or enrichment in biological fluids such as plasma, serum, or urine. Table 1 lists a selection of important biologically active substances of various molecular weights which can be determined by radioimmunological methods. Many of the radioimmunoassays so far developed are already commercially available as analytical kits.

2. Principle of the Method

Radioimmunological methods combine the extreme sensitivity of detection of isotopically labeled compounds (isotopic dilution analysis) with the high specificity of immunological reactions. Thus on use of radioisotopes the detection limit is improved up to 10^7-fold over other physicochemical analytical methods. The *in vivo* and *in vitro* immunological reaction is based on the unique fit of antigen (Ag) and antibody (Ab), which correspond as "lock and key" *(Emil Fischer)*. Given a sufficient binding affinity of the antibody a characteristic equilibrium will be established between the reactants and the resulting water-soluble antigen-antibody complex:

$$Ag + Ab \rightleftharpoons Ag \cdot Ab$$

If the unlabeled antigen (Ag) is replaced by radioactively labeled antigen (Ag*) which differs only slightly, if at all, chemically but not in the slightest immunologically then, by analogy

$$Ag^* + Ab \rightleftharpoons Ag^* \cdot Ab$$

Radioimmunological analyses based on these two equations permit determination of minute amounts of the antigen (Ag) provided that three conditions are fulfilled:

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Table 1. A selection of some radioimmunoassays for various classes of substances.

Name of Substance	Approx. Molecular Weight
1. Peptide hormones	
Vasopressin	1084
Gastrin	2096
Glucagon	3483
Calcitonin (CT)	3700
Adrenocorticotropin (ACTH)	4576
Insulin	5734
Prolactin (PH)	20000
Growth hormone (GH)	21500
Placenta lactogen (PL)	22000
Thyreotropin (TSH)	25000
Luteinizing hormone (LH)	26000
Follicle stimulating hormone (FSH)	30000
2. Non-peptide hormones	
Serotonin	176
Estrogens, androgens, gestagens	300
Prostaglandins	300
Triiodothyronine (T 3)	651
Thyroxine (T 4)	776
3. Enzymes	
Trypsin	23800
Carboxypeptidase A	34000
Pepsinogen	42000
4. Serum proteins	
Thyroxin-binding globulin (TBG)	65000
Albumin	69000
Immunoglohulins (Ig)	150000
5. Vitamins	
Vitamin D_3	385
Vitamin B_{12}	1355
6. Tumor-associated antigens	
Chorion-gonadotropin (CG)	46000
Alphafetoprotein (AFP)	65000
Carcinoembryonal antigen (CEA)	200000
7. Drugs	
Barbiturates	100–200
Morphine	285
Lysergic diethylamide (LSD)	323
Penicillin G	334
Digoxin/Digitoxin	780
8. Other biologically active substances	
Cyclic adenosine monophosphate (c-AMP)	347
Folic acid	441
Deoxyribonucleic acid (DNA)	10^6
Hepatitis-associated antigen (HBAg)	—

1) The antibody (Ab) cannot distinguish between radioactively labeled substance (Ag*) and the unlabeled compound (Ag) to be determined, *i.e.* the binding constant K is the same for the complexes Ag·Ab and Ag*·Ab.

2) More radioactively labeled antigen molecules (Ag*) must be present than antibody binding sites, *i.e.* the number of antibodies (Ab) must be kept at such a level that free labeled antigen (Ag*) is always present besides the complexes Ag*·Ab (even in the absence of unlabeled substance).

3) In a given experimental system the concentration of radioactive compound and the amount of antibody is kept constant for all test runs. The concentration of unlabeled antigen to be determined is thus the sole variable in this system.

Under the above conditions, radioimmunoassay can readily be understood as competitive protein binding analysis. A variable amount of a substance (Ag) and a constant amount of the same radioactively labeled compound (Ag*) compete for a limited and constant amount of binding sites of the antibody (Ab).

Thus all the fewer radioactively labeled molecules (Ag*) will be bound (B) the more unlabeled Ag are present. The

$$\mathrm{Ag} + \mathrm{Ag}^* + \mathrm{Ab} \rightleftharpoons \underset{(B)}{\mathrm{Ag}\cdot\mathrm{Ab} + \mathrm{Ag}^*} \quad \underset{(F)}{\mathrm{Ag}^*\cdot\mathrm{Ab} + \mathrm{Ag}}$$

extent of binding between radioactive molecules and antibodies is thus a measure for the concentration of the compound to be determined.

The situation is shown in drastically simplified schematic form in Figure 1. In all three examples the above requirements are met. The increasing substance concentration in the first vertical series (0, 2, and 6 molecules) at constant amounts of labeled compound and antibody reduces the number of radioactive antigen-antibody complexes (balance). Specificity precludes reaction between other molecules and antibodies. In order to quantitatively establish what proportion of the labeled compound is complexed after equilibration (B), all the antigen-antibody complexes (Ag*·Ab, Ag·Ab) have to be separated from free, unbound antigen (Ag*, Ag). The most important separation procedures are discussed in the light of their advantages and disadvantages in Section 5. After separation and monitoring of the radioactivity of bound (B) or free phase (F) the content of a sample can be read off directly from a calibration curve plotted for standardized amounts of substance.

After mixing of the chemicals and sufficient incubation time a reversible equilibrium is established in the simplest case which can be described by the law of mass action. A plot of the relation derived

$$\frac{[\mathrm{Ag}\cdot\mathrm{Ab}]}{[\mathrm{Ag}]} = K([\mathrm{Ab}]_0 - [\mathrm{Ag}\cdot\mathrm{Ab}])$$

$[\mathrm{Ab}]_0$ = initial concentration of antibody

or expressed in terms of bound (B) and free phase (F)

$$\frac{[\mathrm{B}]}{[\mathrm{F}]} = K([\mathrm{Ab}]_0 - [\mathrm{B}])$$

is a straight line of slope K. This is called a "Scatchard plot"[12] and permits estimation of the binding constant.

However, this approach is grossly simplified and only gives anything like reliable results when the antigen and antibody are chemically uniform and univalent and react as far as equilibration[13]. This equilibrium should not be perturbed by removal of antibody-bound substance from the free species. Moreover, the reaction should be of first order. In practice these conditions are not satisfied. Antisera nearly always contain several populations of antibodies exhibiting different binding strengths, and this heterogeneity alone will prevent us from obtaining linear Scatchard plots[14] and therefore give only "average" binding constants. The real situation becomes even more complicated when it is remembered that cross reactions can occur with chemically similar or structurally related molecules, and several models have been proposed for its exact description and for estimation of its influence on standard curves. These account for, *e.g.*, varying binding behavior of labeled substance, standard substance, and substance to be determined in a biological fluid[15].

Development of a radioimmunoassay and setting up an experimental system first requires that adequate amounts of

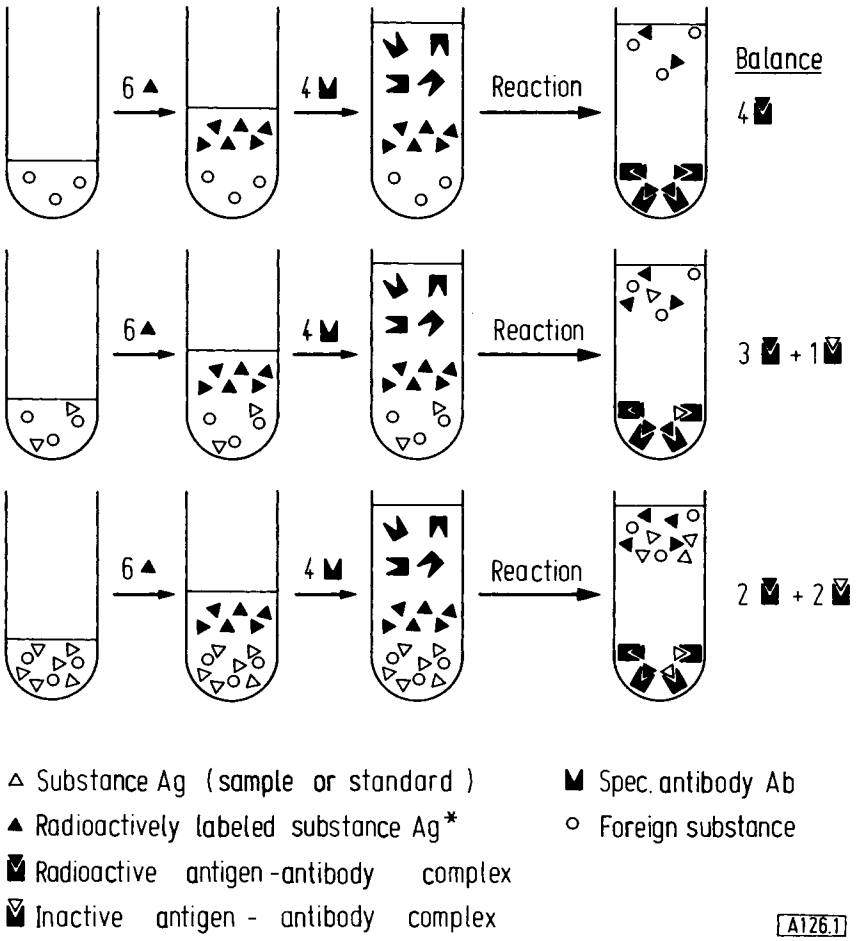


Fig. 1. Schematic representation of the radioimmunoassay principle. A variable amount of the labeled antigen (Ag) and a constant amount of the unlabeled antigen (Ag*) compete for a limited number of binding sites of the antibody (Ab).

the substance to be determined, *e.g.* a hormone, be isolated from biological material and purified or synthesized. After optimum purification a portion of the hormone is radioactively labeled and another portion used for immunization in order to gain antisera, while the unmodified hormone serves as reference for production of a calibration curve. In addition, a suitable reagent is required for separation of antibody-bound hormone from the free hormone.

3. Isotopes and Procedures Used for Radioactive Labeling

The choice of radioisotope and hence the chemical procedure adopted for labeling depends upon various factors. Thus apart from molecular size, structure, stability, and availability of the compound, its purity, retention of immunoreactivity, availability which may be limited in some cases such as hormones, and above all the attainable specific radioactivity all play a significant role. Since the substance to be determined is generally present in nanogram to picogram amounts in the samples, a precise radioimmunological determination is only possible if the amount of labeled substance (tracer) itself is kept very small. Thus to assure a satisfactory detection sensitivity for reasonable measuring times a tracer having an adequate specific radioactivity will be required. A tracer activity of between 100 and 200 mCi/mg will suffice for most radioimmunoassays. About 10 nCi (*ca.* 22000 decays per minute) corresponding to about 60 pg of labeled substance, and sometimes even less, is added to each test tube.

Of all available radioisotopes, preference would be given to ^{14}C for labeling organic substances because the ^{14}C-tagged compounds behave in exactly the same way as the starting compounds. As shown by Table 2, however, the specific radioactivity attainable with ^{14}C is so low that at best 0.1 μg of a substance can be determined. Another disadvantage is that ^{14}C labeling usually requires several synthetic steps and frequently gives only low yields. In addition, ^{14}C labeling is simply impossible for numerous complicated or polymeric natural products such as polypeptides, proteins, and glycoproteins which have hitherto resisted synthesis and are often only available in minute quantities.

Owing to the shortcomings of ^{14}C, relatively small molecules such as steroids, prostaglandins, or drugs are tagged with tritium. The radioactivity is usually introduced by catalytic tritiation of double bonds, by Wilzbach tritiation or by an exchange reaction, *e.g.* halogen for tritium. Tritium compounds also display various disadvantages which preclude their general application. Thus the specific radioactivity is often too low, while tritium compounds of higher activity are relatively unstable. Moreover, recording β-radiation in a liquid scintillation counter involves preparation of a "scintillation cocktail", a complicated and expensive procedure.

Most commonly, an extraneous label is used for radioactive tagging, or in the case of compounds like thyroid hormones

Table 2. Theoretical maximum possible specific radioactivity of a compound when 1 atom of the isotope is incorporated in the molecule.

Isotope	Radioactivity [Ci/mmol]	Half-life	Radiation
^{14}C	0.062	5568 a	β^-
^{3}H	29	12.3 a	β^-
^{75}Se	1080	120.4 d	γ
^{35}S	1488	87 d	β^-
^{125}I	2200	59.7 d	γ
^{131}I	16100	8.1 d	β^-, γ

which contain iodine an exchange labeling with ^{125}I is carried out. This γ-emitter permits labeling of an intact molecule in one step and affords a product of high specific radioactivity (Table 2). Thanks to its long-half-life of 60 d, ^{125}I has almost completely ousted ^{131}I, which is nowadays used practically exclusively for *in vivo* studies.

Iodination is limited to compounds which, like nearly all peptides and proteins, contain the amino acids tyrosine or histidine. It should also be borne in mind that incorporation of iodine into the molecule may cause *inter alia* a change in conformation whose magnitude will depend upon the size of the molecule; hence it may be bound less firmly if at all by the antibody owing to changes in its immunological properties. Such changes in binding properties can be seen directly from a comparison of the immunoreactivity of tracer and unlabeled compound.

Iodine labeling is based upon electrophilic substitution in the activated aromatic ring, *e.g.* in *ortho* position to the hydroxyl group in tyrosine. Practically all procedures developed for this purpose differ merely in the oxidizing agent used for producing radioactive iodine from the ^{125}I anion. In this reaction the substance to be labeled is already present and therefore exposed to the oxidizing agent. This leads to interference by oxidation-sensitive SH groups and amino acids, and hence to undesired changes in the molecule. Use of exceptionally mild oxidizing agents and very short reaction times of 5 to 60 seconds, however, keeps the proportion of degradation products very small or permits their removal by purification of the reaction mixture. Reaction is usually stopped by a reducing agent such as sodium disulfite ($Na_2S_2O_5$) or by dilution with buffer solution.

Of all procedures, the chloramine T method[16, 17] of iodination with a few microgram of substance has found the widest acceptance. In comparison the number of examples in which labeling is performed with iodine monochloride[18, 19], with gaseous chlorine[20], with sodium hypochlorite[21], or by electrolytic means[22] are of minor importance. Increasing use is being made of enzymatic iodination with lactoperoxidase[23] or horse radish peroxidase[24, 25]. Procedures involving activated esters are particularly mild[26, 27]. Thus in a reaction preceding the acylation, for example, 4-[2-(succinimidooxycarbonyl)ethyl]phenol ["*N*-succinimidyl-3-(4-hydroxyphenyl)-propionate"] is radioactively labeled by the chloramine T method, the iodinated compound purified and subsequently allowed to react with free amino groups of the peptide or protein. The procedure has the advantage that sensitive substances do not come into contact with ^{125}I or the reagents required for iodination. Moreover, it provides a means of tagging compounds containing *neither* tyrosine *nor* histidine.

In order to utilize the advantages, *i.e.* high specific radioactivity and simple measurement, of iodine-labeled compounds with low-molecular substances, these haptens (see Section 4) are coupled *via* a bridging group with iodinatable auxiliary compounds such as tyrosine esters, tyramine, or histamine[28, 29]. It should be noted, however, that the new compounds often display completely different immunological properties from the starting compound, which, in extreme cases, can lead to a complete loss of binding to the antibody. The site of linkage between the substance and the auxiliary compound therefore warrants particular attention.

Instead of using these conjugate systems, which can considerably alter both the size and the structure of the molecule, it has meanwhile become possible to directly label steroids with ^{75}Se (Table 2)[30].

After the labeling operation with ^{125}I, the radioactive compound should be immediately removed from the reaction mixture of unreacted ^{125}I, radiation-damaged products, and inactive components. Since the amounts involved are usually of the order of 10 to 50 µg, purification is possible only with effective separating systems such as gel filtration, gel electrophoresis, chromatography, or selective adsorption. After purification the substance is tested for radiochemical homogeneity by chromatography or electrophoresis (Fig. 2).

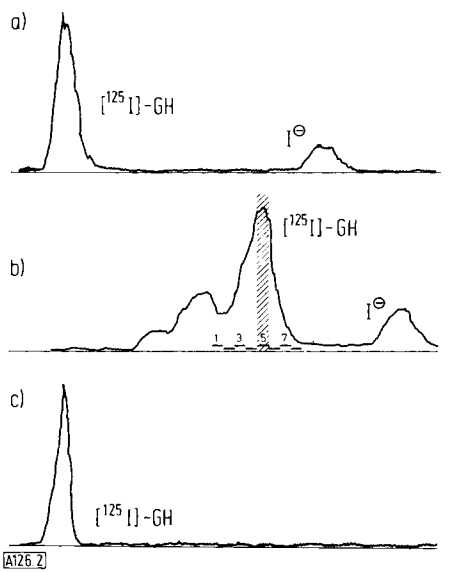


Fig. 2. Purification and testing of ^{125}I-labeled growth hormone [^{125}I-GH]. a) electrophoresis of the reaction mixture; b) purification by gel filtration; c) electrophoresis of fraction 5.

The radiochemical purity of the labeled compound steadily decreases on prolonged storage due to autoradiolysis, *i.e.* modification by radiation and loss of iodine atoms. Decomposition can be kept low and the shelf-life improved by reducing the activity concentration and also by addition of albumin and buffer. A further improvement in stability can be achieved by storage at low temperature (−20 °C) and by freeze-drying of the product.

4. Formation and Properties of Antibodies

Antibodies are endogenous glycoproteins and are regarded as carriers of protection against infection. They are formed in the pertinent lymphoid cells (plasma cells) of the organism on intrusion of an extraneous substance and secreted into the blood circulation. Complex formation with the antibody renders the antigen harmless.

On electrophoresis of serum, antibodies migrate with the γ-globulin fraction. Because of their extensive functional and structural resemblance to γ-globulins they are called immunoglobulins (Ig). They have molecular weights between 150000 (IgG) and 900000 (IgM) and generally consist of two long and two short chains which are linked together by disulfide bridges[31-33].

An essential characteristic of antibodies is the specific binding with the antigen which induced their formation. The reason for the specificity can be seen in the spatially fitting complementary configurations of the antigen determinant groups and the binding groups on the immunoglobin molecule. If the serum containing the antibodies, and therefore known as antiserum, is isolated the antigen-antibody reaction usually occurring *in vivo* can also be employed for quantitative determinations *in vitro*.

Antibody formation depends upon several factors, the most important ones being the form of the antigen offered and the animal species selected for immunization. Species-foreign proteins having a molecular weight in excess of 5000 generally act as antigens. Thus even a slight difference in amino acid sequence or a single amino acid substitution, *e.g.* in insulin, can suffice to produce antigenic properties. Smaller molecules such as the polypeptides gastrin or vasopressin, steroids, thyroid hormones, and drugs, have only little, if any antigenic action. However, antibodies can also be produced against these haptens by linking them in covalent manner to high molecular carriers. The compounds are coupled *via* short bridges (four to six CH_2 groups) to natural or synthetic proteins or polymers such as albumins[34], polylysine[35], or polyethylene glycol. The attached minor molecule (determinant group) then determines the specificity of the antibody, *i.e.* the latter does not react with the complete antigen molecule but with only a small part thereof, the hapten. However, the position at which the hapten molecule is linked to the carrier protein is of crucial importance for the specificity of an antiserum[36]. Positions having functional groups in their immediate vicinity, *e.g.* rings A and D in steroids, should not be changed on conjugate formation.

Animals suitable for immunization are rabbits, as well as guinea pigs, sheep, and goats. In general several animals are immunized simultaneously, the amount of immunogen (antigen) or hapten conjugate depending on the substance and the animal. The substance and the animal also determine the kind of injection (*e.g.* intravenous, subcutaneous, intramuscular), the additives (complete or incomplete Freund's adjuvant), and the time intervals between boosters[37, 38].

Between two injections, serum must be taken and examined to establish whether antibodies have already been formed and if so what quality they have. Since antibodies are even degraded at different rates during immunization the ideal time for bleeding the animals can only be established by constant surveillance. The sera taken from the animals can be used directly without special treatment after corresponding dilution.

The most important criteria for assessment and choice of an antiserum for radioimmunoassay are titer and specificity. By convention, the titer is that antiserum dilution at which 50 % of the offered tracer are bound under standard conditions. Figure 3 shows a dilution curve for an anti-T3 serum obtained by immunization of a rabbit with T3-BSA conjugate (3,3',5-triiodothyronine bovine serum albumin).

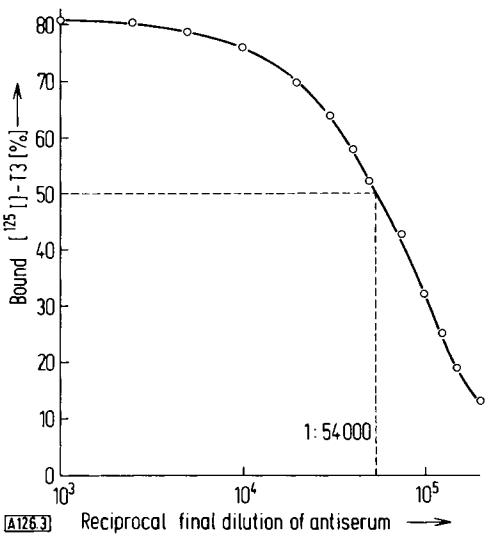
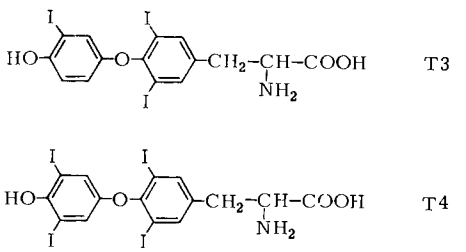


Fig. 3. Antiserum dilution curve for assessing the working concentration (titer) for 50 % binding of tracer.



Although the antigen-antibody reaction is exceptionally specific, interference by extraneous molecules must always be reckoned with. These cross reactions are due to molecules of similar structure or those that are closely related. Thus an antibody generated by growth hormone (GH, peptide chain with 190 amino acids) also reacts with placenta lactogen (PL, peptide chain with 191 amino acids), or anti-T3 serum also with the thyroid hormone thyroxine (T4) (Fig. 4).

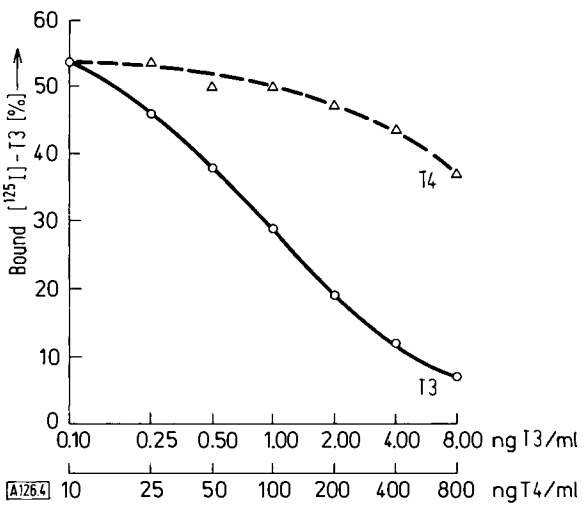


Fig. 4. Determination of specificity of an antibody. Cross reaction of an anti-T3 serum *versus* the structurally related thyroid hormone thyroxine (T4).

To what extent cross reactions can be neglected must be decided from case to case, and is also determined by the

physiological concentration. In the healthy body the thyroid hormones T3 and T4 are present in the ratio 1:50 to 1:100; hence a cross reaction of anti-T3 serum with T4 of only 1% would suffice to seriously falsify a T3 determination. Only an antibody exhibiting an extremely slight cross reaction with T4 (<0.1 %) will give accurate values for T3, as shown by Figure 4.

Antisera can be stored either undiluted or diluted with buffer and frozen to −20°C. To avoid repeated thawing and freezing, the valuable antiserum should be divided up into small portions just sufficient for a series of samples. They become particularly suitable for storage if lyophilized in a dilution suitable for performing the assay. Storage of such preparations is feasible at 2 to 8°C and they remain active for a considerable time.

5. Methods of Separating Antibody-Bound and Free Antigen

After equilibration of the incubation mixture of the reactants Ag, Ag* and Ab, *i.e.* after extensive saturation of the antibody, it remains to establish what percentage of the added radioactive compound has been complexed. This is accomplished by isolating the antibody-bound portion (B) from the free, unbound antigen (F) (see Section 2). It is in the method and execution of this separatory step that the greatest differences are found between the radioimmunoassays so far reported. This is manifested in a whole variety of separation methods, of which the most important are listed in the order of their efficacy in Table 3.

Table 3. Methods and materials for the separation of antibody-bound and free antigen.

Separating action	Method/Material
Partition of the components due to their different mobility and molecular size	Chromatography Electrophoresis Gel filtration Ultracentrifugation
Precipitation of the Ag·Ab complex	Ammonium sulfate Sodium hydrogen sulfite Zirconyl phosphate Ethanol 2-Propanol Dioxane Polyethylene glycol (PEG)
Adsorption of the antigen	Charcoal (also bound to dextran or albumin) Cellulose Silicates Ion-exchange resins
Binding of the antibody to a solid phase	Antibody chemically bound to polymer carrier (ASP) Coated tubes or beads
Immunological complex formation with a second antibody	Double antibody method (DA) Second antibody chemically bound, *e.g.* to activated cellulose (Immunosorbent, DASP)

Separation mainly exploits the properties of the complex, which however show extensive agreement with those of the antibody. Thus the antigen-antibody complexes can very readily be separated from unbound antigen on the basis of molecular size or limited solubility at certain pH values, by way of differing migration rates, by denaturation and precipitation with salt solutions or with organic liquids. Separation could also utilize a further subsequent immunological reaction, in which a second antibody directed against the first antibody, and hence also against the antigen-antibody complex, forms a much larger high-molecular complex. Methods are steadily gaining ground in which the second antibody and in some cases even the first antibody is physically or chemically bound to a solid phase.

A comparative study of the separatory methods is difficult, and it must usually be left to the judgment of the user as to which one of several methods he prefers.

It is essential that two conditions be fulfilled when choosing a method or testing a new separating agent:

1) The separating agent should not interfere with the equilibrium state of the completed reaction, *i.e.* the antigen-antibody complexes must be preserved during the separation.

2) The antibody-bound molecules and the free unbound molecules must be quantitatively separated from one another.

In order to meet both requirements, the separating agent and the separating reaction must both be highly specific. The resting state of the immunological equilibrium or saturation reaction should not be affected, even after prolonged action or reaction times or at various temperatures. The most suitable reagents are therefore those which do not undergo non-specific binding with the radioactively labeled compound and thus cannot cause an undesired co-precipitation. Moreover, the two phases should be separable from each other reliably, fast, simply, and without any great experimental effort. Apart from the above effects, other factors such as composition and concentration of the buffer, the pH values, addition of albumin, and the make-up of the serum also play a role. All these factors require careful testing, particularly with regard to the amount of separating reagent and reaction time.

A frequently employed separation method is shown schematically in Figure 5 (see also Table 3). Apart from the known protein precipitants such as ethanol, 2-propanol, ammonium sulfate solution, and more recently polyethylene glycol, importance also attaches to adsorption agents in which the separatory action arises from adsorption of the free antigen. Among the latter, charcoal and charcoal bound to supports have been widely used because of their great adsorption potency; however, they often exhibit the undesired effect of releasing the antigen from the complex and adsorbing it. On use of charcoal suspensions these effects must be minimized by working at low temperature (4°C) and short reaction times of equal duration.

In the double antibody technique the antigen-antibody complex is completely precipitated by an addition of a second antibody directed against the first antibody. However, this method is often critical, requires centrifuges having high *g* number, and some degree of practice. More reliable and easier to perform in practice is the method in which the second antibody is covalently bound to a solid phase, *e.g.* to cellulose[39]. These immunosorbents are highly stable and can be used against all antibodies of a particular animal species. They are added to the reaction mixture as a suspension, give readily visible precipitates, and are characterized by extremely low nonspecific binding.

Another method that is simple in operation is carried out in polystyrene test tubes whose walls are coated with antibody; alternatively the coating may be applied to small plastic spheres or discs. Separation is then accomplished simply by

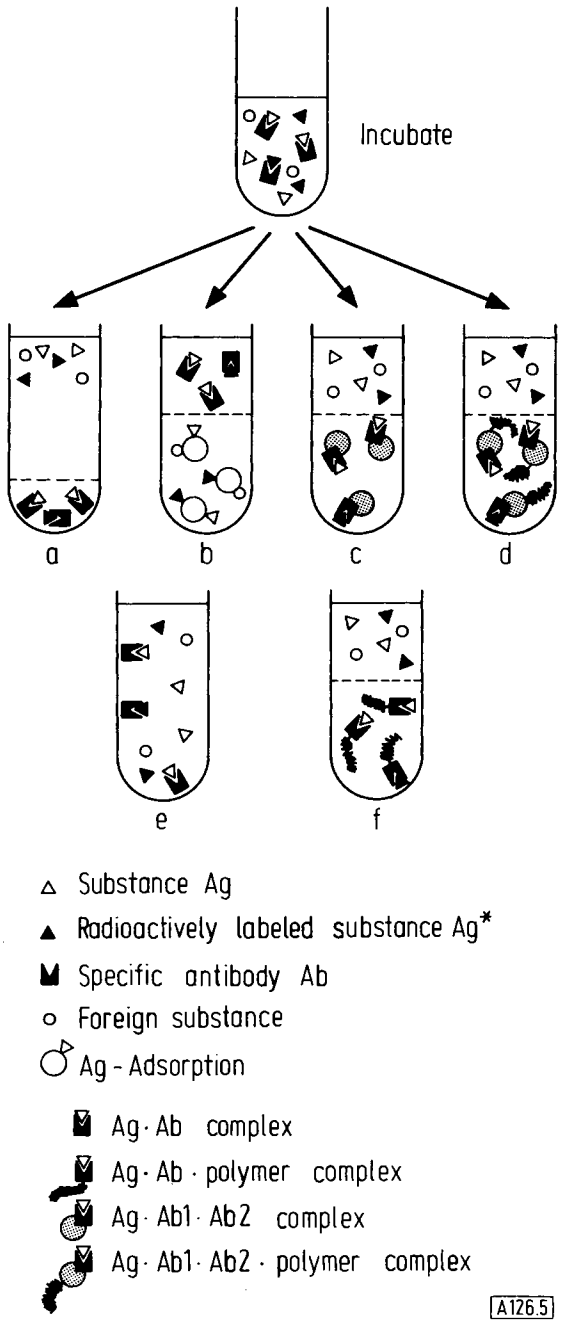


Fig. 5. Schematic representation of the separatory action in radioimmunoassay for the determination of antibody-bound and free substance. a) protein precipitation; b) adsorption agent; c) double antibody (DA); d) immunosorbent (DASP); e) antibody adsorptively bound to the surface; f) antibody chemically bound to polymer.

pouring out the reaction mixture. However, the coatings require large amounts and high concentrations of valuable antiserum, and difficulties are sometimes encountered in ensuring uniform quality. Finally, some radioimmunoassays are known in which the first antibody is already chemically bound to activated polymers, thus permitting direct separation of free and bound substance on completion of the reaction.

In all separating operations, intimate mixing of separating reagent with the incubated reaction mixture and completion of the reaction, which can take minutes or hours, is followed by centrifugation and separation of supernatant from residue. The final operation consists in monitoring the radioactivity of one of the two phases—sediment or supernatant.

6. Execution of Measurement and Evaluation of Results

So far all radioimmunological determinations require plotting of a calibration curve. Furthermore, it is also necessary to include a sample of known content as a check, *e.g.* when determining a hormone in serum.

On execution of a radioimmunoassay exactly equal volumes—generally 100 µl—of the standard solutions of various concentration and of the samples are pipetted into test tubes of *ca.* 2 to 4 ml capacity. The test tubes are usually made of polystyrene or polypropylene and are only used once. To each run are then added exactly equal amounts, *e.g.* 100 or 200 µl, of a solution containing radioactively labeled substance and the dilute antibody solution. Adsorption of reaction components on the walls of the test tubes, and consequent spurious results, are avoided by buffering all solutions and frequently also by addition of albumin as carrier protein.

In general, all determinations are performed in duplicate and sometimes, especially when plotting the calibration curve, even in triplicate. Use of metering pumps, dilution equipment (dilutors, dispensers), and automated pipetting apparatus permits rationalization of most experimental steps. Recent years have seen the development of partly and fully automated analytical systems for routine determinations, which are especially suitable for radioimmunoassays utilizing the same separation technique, *e.g.* the double antibody method or gel filtration[40, 41].

The test tubes have to be incubated for several hours to several days under the most favorable reaction conditions, which have to be determined on working out an assay. Subsequently the free species must be separated from the antibody-bound substance and the reactivity of one of the phases recorded in a "γ-counter" or in the case of ^{3}H-labeled compounds in a liquid scintillation counter. These experimental values permit plotting of the calibration curve and thence the determination of the sample.

Depending upon the kind of plot, the calibration curves have different forms (straight line, hyperbola, sigmoid). For example, the number of counts recorded, the percentage of absolute or of relative binding can be plotted against the concentration or the logarithm of the concentration. Apart from manual methods, mechanical techniques are also suitable for evaluation, of which the logit-log transformation, where the curve is more or less linearized and particularly smoothing by a spline function[42, 43] have proved of value. Which of the numerous methods is employed for evaluation will depend upon the individual radioimmunoassay, and also on the number of samples to be evaluated. However, it is always necessary to plot a calibration curve, even on mechanical evaluation, and to subject its shape to critical scrutiny.

In order to ensure reliability of the results obtained, and thus to guarantee the quality of a radioimmunoassay it is necessary to know a number of characteristic data. These include the specificity and sensitivity, and above all the accuracy, reproducibility, and precision of an assay.

As already mentioned, the specificity of a radioimmunoassay is essentially determined by the antibody. It can be impaired by cross reactions with similar substances and fragments thereof, and also by the separating step. Serum factors, pH value, additives such as albumin, buffer, heparin, or preservatives can also lower the specificity.

Another criterion for assessing a radioimmunoassay is its sensitivity. This signifies the lowest concentration that can be significantly detected. The sensitivity depends upon the specificity of the antibody and is the higher the greater the specific radioactivity of the tracer or the less there is of it in the experimental run. The sensitivity can be regarded as the special case of the accuracy at zero concentration. In practice, the lower detection limit can be established, *e.g.* by subtracting the 3s deviation of the scattering from the initial binding value and reading off the relevant concentration from the calibration curve. The sensitivity of assays in which the immunological reaction is irreversible or measurement is performed at non-equilibrium can occasionally be raised by delayed addition of the radioactively labeled substance ("cold" pre-incubation)[44].

The accuracy attainable in a determination depends upon three errors of various magnitudes. Apart from experimental errors arising in several pipetting steps and interference of the reaction (*e.g.* varying degree of wall adsorption), errors also occur in measuring the radioactivity (*inter alia* statistical error of radioactive decay) and on evaluation of the various samples. Owing to the different nature of these errors, it is clear that the accuracy cannot be the same in each portion of the curve. However, multiple determinations and long counting times can do much to reduce random errors and thus lead to a more accurate result.

A further criterion of quality is reproducibility. Duplicate or multiple determinations on samples of an assay and the resulting deviations from the average value yield the intra-assay reproducibility. It normally lies below 5%. The inter-assay reproducibility is the coefficient of variation obtained on determination of the same sample in several different assay runs using different reagents. Its value lies below 10% for accurate and reproducible radioimmunoassays[45].

It is particularly difficult to assess whether the value found by radioimmunology is the precise value, *i.e.* identical with the unknown true value. In this context it should be pointed out that only the amount of immunologically active substance can be determined. This is not necessarily identical with the amount of biologically active substance. Comparison of normal and abnormal values from various laboratories is feasible only after adjusting one's own standard to an international reference standard[46].

Checks on precision are also possible with test sera determined at various dilutions and recovery measurements in which a known amount of substance is added to a sample. Determination of the sample with and without added substance will reveal whether sample effects falsify the result.

7. Radioassay and Immunoradiometric Assay

Radioassays and variants of immunoradiometric assay (IRMA)[47] are techniques closely related to radioimmunoassay. In radioassay a carrier or transport protein already present in the organism serves as binding partner instead of an antibody. Two radioassays used in thyroid diagnosis, in which thyroxine-binding globulin (TBG) serves as binding reagent, possess immense practical importance.

After secretion by the thyroid the two hormones thyroxine (T4) and triiodothyronine (T3) (see Section 4) are bound almost completely by serum proteins, especially TBG. Thus the TBG binding capacity which can be determined with the radioactive indicator [^{125}I]-T3, provides an indirect measure of thyroid activity. Just as in radioimmunoassay, the bound [^{125}I]-T3 must be isolated and monitored after saturation of the free binding sites. Determination of T4 is based on the fact that it can displace [^{125}I]-T4 from a labeled [^{125}I]-T4-TBG complex to an extent depending upon its concentration. After equilibration, the liberated [^{125}I]-T4 is separated from the complex, *e.g.* with an ion exchanger, and its radioactivity monitored.

$$Ag + Ab^* \rightleftharpoons Ab^* \cdot Ag$$
$$Ab^* + Ag\text{-polymer} \rightleftharpoons Ab^* \cdot Ag\text{-polymer}$$

In contrast to radioimmunoassay, in the immunoradiometric assay it is the antibody and not the antigen which is radioactively tagged and added in excess to the test run. Because of this excess, all antigen molecules are bound by antibodies at the conclusion of reaction, and it is necessary to separate antigen-antibody complex and excess antibody. Apart from a series of advantages, such as greater stability of the iodinated antibody as compared to the labeled antigen, high attainable specific radioactivity (without loss of immunoreactivity) and the high sensitivity in assays for high-molecular compounds, the method also has some drawbacks. Thus the slight difference in size between antibody and antigen-antibody complex often makes separation difficult. It is therefore carried out with an immunosorbent in which the antigen is bound to a polymeric carrier. The antibodies must also be bound to this immunosorbent during iodination, and then released again. These steps are usually accompanied by losses, so that relatively large amounts of the valuable antiserum are required.

If the antigen can bind to two antibody molecules then the sandwich technique (two-site assay) can be implemented. The antigen to be determined is initially allowed to react with an immobilized antibody, the resulting complex washed, and then incubated with the radioactively labeled antibody in a second reaction. This procedure affords a labeled antibody*-antigen-antibody-polymer complex.

The hepatitis B virus antigen (HB·Ag) assay on human serum, one of the commonest immunoradiometric determinations performed, is based on this sandwich technique.

8. Summary

In recent years radioimmunological techniques have greatly improved our understanding of endocrine physiology. These methods are superior to most other analytical procedures, both in diagnosis and in surveillance of therapy, with regard to sensitivity, specificity, general applicability, and experimental simplicity. Routine applications of radioimmunoassay extend beyond biochemistry and clinical chemistry into microbiology, toxicology, and virology, as well as studies on drug metabolism. Applications in early diagnosis of cancer and in monitoring of tumor diseases after therapeutic measures can also be envisaged.

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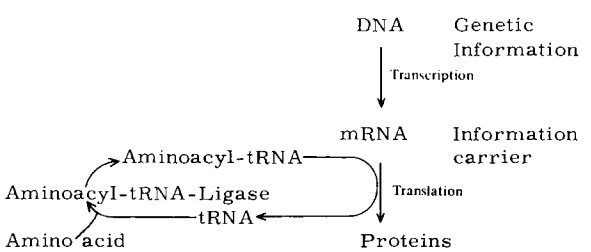
Chemical Methods of Studying Ribosome Structure

By Ernst Küchler[*]

The use of chemical methods, and in particular affinity labeling, has greatly advanced our knowledge about the structure of the active sites of ribosomes. Experiments have shown that ribosomal proteins and ribosomal ribonucleic acids participate in the structure of the binding sites for messenger ribonucleic acid and transfer ribonucleic acid.

1. Introduction

The genetic information of a living cell is recorded in a long filamentous molecule, deoxyribonucleic acid (DNA). DNA does not directly participate in cellular processes, but merely stores information. In order to find expression the genetic information must first be transcribed into a ribonucleic acid (RNA). Because of its information-carrying function this RNA is called messenger RNA (mRNA).



Apart from mRNA, the cell also contains transfer ribonucleic acids (tRNA) and ribosomal ribonucleic acids (rRNA), which have other functions. The nucleotide sequence of mRNA is translated into the amino acid sequence of proteins on the ribosomes. Each group of three consecutive nucleotides is read as the signal for incorporation of a particular amino acid; this sequence of three nucleotides is termed a codon. The key molecules for translation are tRNAs, there being one or more tRNA species for each amino acid occurring in proteins. Binding of the amino acid to the tRNAs is effected by specific enzymes, the amino acyl tRNA ligases; on addition of the amino acid to the protein chain the amino acyl tRNA is "discharged" and can then be amino acylated afresh.

The nucleotide sequence of a codon in the mRNA is recognized by the tRNA by interaction with a nucleotide sequence known as the anticodon. The interactions between codon and anticodon arise by base pairing between the complementary nucleotides (nucleoside monophosphates) adenylic (AMP) and uridylic acid (UMP), and guanylic (GMP) and cytidylic acid (CMP).

tRNAs have chain lengths of 75 to 80 nucleotides. Apart from AMP, CMP, GMP, and UMP (only the nucleosides

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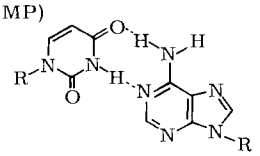
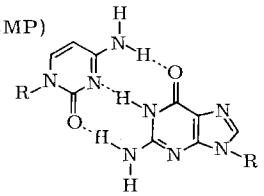
Uridylic acid (UMP)



Adenylic acid (AMP)

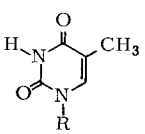
Cytidylic acid (CMP)



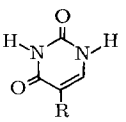
Guanylic acid (GMP)

R = Ribosyl phosphate

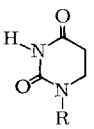
are usually given: A, C, G, and U) they also contain "rare" nucleotides, of which ribothymidylic (TMP), pseudouridylic (ΨMP), and dihydrouridylic acid (DMP) may be cited as examples.



Ribothymidylic acid (TMP)



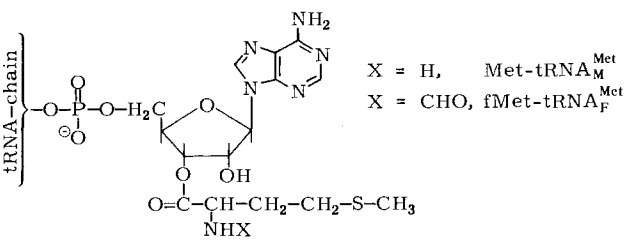
Pseudouridylic acid (ΨMP)



Dihydrouridylic acid (DMP)

R = Ribosyl phosphate

The nucleotide sequence of the tRNA determines its specificity. However, some nucleotide sequences are common to all tRNAs; thus, all tRNAs contain the sequence TΨC at the same position in the polynucleotide chain. Furthermore, the sequence –CCA is always found at the 3′ end of tRNAs. In the amino acyl tRNA the amino acid is linked *via* an ester bond with the ribose of this terminal adenosine. The amino group of the amino acid is therefore free and can be linked *via* a peptide bond to the growing protein chain on the ribosome.



X = H, Met-tRNA$_M^{Met}$
X = CHO, fMet-tRNA$_F^{Met}$

The tRNAs specific for methionine represent a special case. In addition to methionyl tRNA (Met-tRNA$_M^{Met}$) there is also a formylmethionyl tRNA (fMet-tRNA$_F^{Met}$), in which the amino group is "blocked" by a formyl group. This tRNA serves as initiator tRNA. The biosynthesis of all bacterial proteins thus begins when a formylmethionyl group becomes available as the N-terminus of the protein. This formylmethionyl group is removed at a later stage. Specific initiation and termination codons serve as "start" and "stop" signals. The individual steps of the translation of mRNA have received detailed consideration in an earlier review[1] and will therefore be considered only insofar as is necessary for an understanding of ribosome topography.

Ribosomes are cell organelles composed of two subunits, each consisting of rRNA (ribosomal RNA) and proteins. The subunits and the rRNA species are named according to their sedimentation constants. The 30S subunit of the bacterial ribosome having a particle weight of 900000 daltons (D) contains a 16S RNA (550000 D) together with a total of 21 different proteins. The proteins are designated S1 to S21 (S = small subunit)[2]. A more complex composition is found in the 50S subunit. It contains two RNA species, 23S RNA (1100000 D) and 5S RNA (40000 D), and no fewer than 34 different proteins, designated L1 to L34 (L = large subunit)[2]. The complete bacterial ribosome (70S) possesses a particle weight of 2650000 D. Ribosomes from the cells of higher organisms are considerably larger; their particle weights are 4000000 D. However, present-day knowledge appears to indicate that their structures are very similar. In this article we shall restrict our attention to bacterial ribosomes, taking the bacterium *Escherichia coli* as example.

The reason for the size and complexity of ribosomes is probably to be seen in the numerous catalytic functions and events which occur on these organelles with participation of ribosomal components and reversibly bound factors.

Initiation of translation of the mRNA nucleotide sequence into the amino acid sequence of the protein involves not only the fMet-tRNA functioning as initiator but also three initiation factors (IF1, IF2, IF3)[3]. The trinucleotide sequences AUG and GUG serve as initiation codons. To the 30S subunit, containing fMet-tRNA$_F^{Met}$, guanosine triphosphate (GTP), mRNA, and the initiation functions IF1 and IF2, is added the 50S subunit, whereupon the initiation factors are released with concomitant hydrolysis of GTP to guanosine diphosphate (GDP) and phosphate (P_i) (Fig. 1)[4–6].

Following initiation, the amino acyl tRNA (generally: AA-tRNA) corresponding to the next codon will be bound. This involves interaction between the anticodon of the tRNA and the codon of the mRNA, on the one hand, and between the TΨC sequence of the tRNA with a complementary GAA sequence of the ribosomal 50S RNA[7], on the other. The process is catalyzed by the elongation factor EF-Tu, and is accompanied by hydrolysis of a further GTP molecule. The ribosome accordingly possesses binding sites for two molecules of tRNA (see Fig. 1), which are called donor and acceptor site (the term "peptidyl site" is also used synonymously with "donor site"; we prefer the former designation, however, as a more fitting description of its function in peptide elongation).

On formation of the first peptide bond, the formylmethionyl group is transferred from the fMet-tRNA$_F^{Met}$ located at the donor site to the amino acyl tRNA (AA-tRNA) in the acceptor site. A dipeptidyl-tRNA is formed, the reaction being catalyzed by the ribosome itself. The corresponding enzymatic activity—known as peptidyl transferase—is located in the 50S subunit[8]. Before undergoing further elongation the resulting dipeptidyl-tRNA must first be transferred from the acceptor site to the donor site, in order to vacate the acceptor site ready for the next amino acyl tRNA. This process, in which the mRNA also shifts by the length of a codon relative to

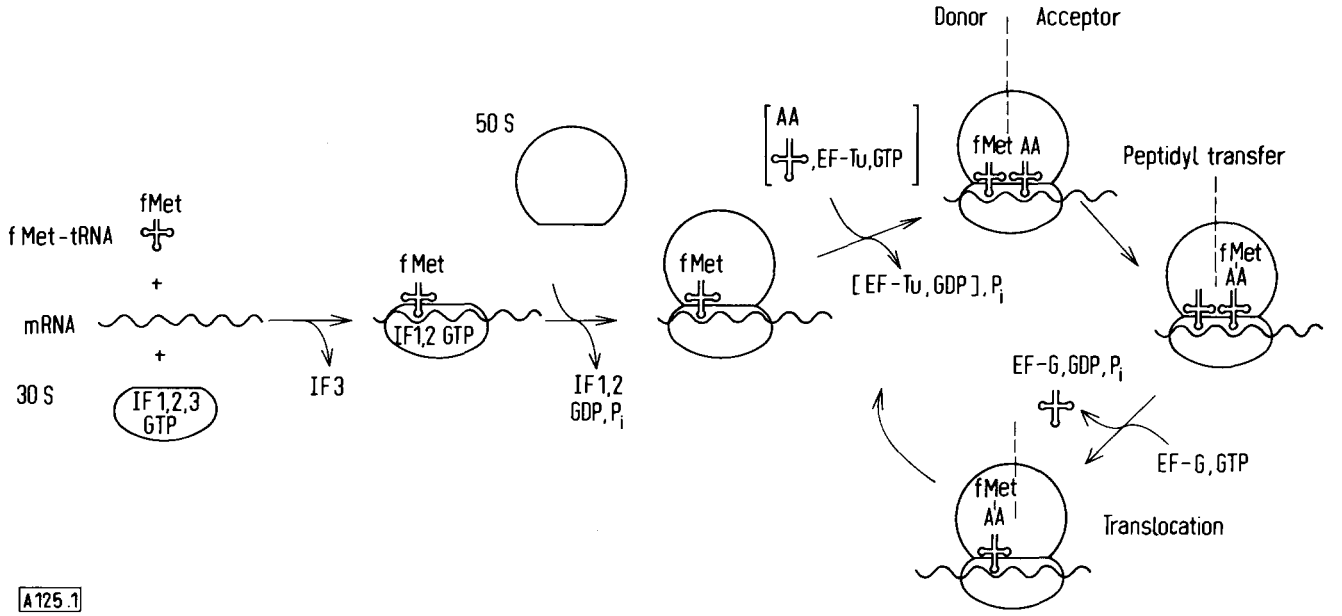


Fig. 1. Scheme of initiation and translation in protein biosynthesis. See text for explanations of abbreviations.

the ribosome, is called translocation. The participating elongation factor EF-G is released after translocation and GTP hydrolysis (see Fig. 1). The ribosome can now bind the amino acyl tRNA corresponding to the next codon with the aid of EF-Tu and GTP to the acceptor site and then repeat the entire cycle again and again until a termination codon appears in the mRNA. The binding sites for EF-Tu and EF-G on the ribosome partially overlap, thus precluding simultaneous attachment of the two factors[9].

The antibiotic puromycin acts as an analog of amino acyl tRNAs[1]. It is bound to the acceptor site and can react with fMet-tRNA$_F^{Met}$ or a peptidyl tRNA located at the donor site to form a peptide bond. The resulting puromycin derivative is released from the ribosome; hence, puromycin effects an artificial termination.

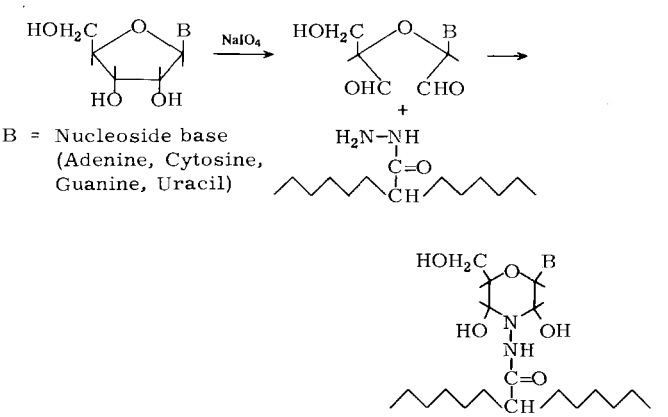
The termination codons UAG, UAA, or UGA could be recognized by the ribosome itself[10] or by the termination factors R 1 and R 2[11]. Chain termination presumably occurs by transfer of the peptide chain to H_2O with the aid of peptidyl transferase[12].

Accordingly, the ribosome must possess binding sites not only specific for tRNA and mRNA, but also for initiation, elongation, and termination factors. Moreover, it must also provide a hydrophobic environment which prevents abortive transfer of the peptide chain to H_2O as a side reaction during transpeptidation on the one hand and enhances interactions between the nucleotides by exclusion of water on the other.

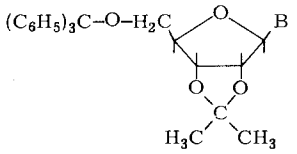
2. Base Pairing between Complementary Nucleosides in Aqueous and Nonaqueous Media

Attempts to directly demonstrate interactions between complementary nucleotide bases in aqueous solutions date back to the initial studies on DNA structure by *Watson* and *Crick*[13]. They long remained unsuccessful because in the absence of the base stacking occurring in the polymers, and as a result of competition of the H_2O molecules in hydrogen bonding, the interactions are so weak that they cannot be detected by conventional physicochemical methods.

In biological systems—such as on biosynthesis of DNA, RNA, and protein—the interactions between nucleotides or short nucleotide sequences probably always take place with partial exclusion of water in the "hydrophobic pockets" of the proteins. Such conditions can be simulated for physicochemical studies by covalent binding of a base to an insoluble carrier material or by use of solvents having low dielectric constants. Base pairing could be detected in both cases.



In order to perform affinity chromatography in an aqueous buffer system, nucleosides were oxidized by periodate to dialdehydes which were covalently bound to the hydrazide groups of an insoluble support material. Mixtures of nucleosides in aqueous buffer were chromatographed over these "nucleoside columns". It was found that uridine is retarded relative to cytidine on "adenosine columns", whereas cytidine is retained more than uridine on "guanosine columns"[14,15]. The same result is obtained on chromatography of the deoxynucleosides thymidine and deoxycytidine, thus showing that the observed effects are attributable to specific interactions between the complementary bases adenine and uracil (or thymine) and between guanine and cytosine. This finding is substantiated by the disappearance of these interactions on replacement of the H atoms participating in hydrogen bonding by methyl groups[16].



B = Nucleoside base (Adenine or Uracil)

Base pairing *via* hydrogen bonds can be observed particularly readily by IR spectroscopy[17]. 2',3',*O*-Isopropylidene-5'-*O*-trityl derivatives of nucleosides in which all OH groups of ribose are substituted dissolve in organic solvents. Since the IR bands of free H atoms and those involved in hydrogen bonding differ, it is possible to determine the binding constants for base pairing. We have established that in CCl_4 the adenosine and the uridine derivative are associated in the ratio 1:1. The tendency of the nucleoside derivative to engage in self-association is much weaker. Various association constants are listed in Table 1. It may be seen that the adenine-uracil base pair is about six times more stable than are the uracil-uracil and adenine-adenine pairs. These findings accord with the results of other authors[18].

Table 1. Association of the 2',3'-*O*-isopropylidene-5'-*O*-trityl derivatives of adenosine and uridine in CCl_4 at 20°C.

Mode of association of derivatives	K_{Ass} [liter/mol]
Uridine-Uridine	1.1×10^2
Adenosine-Adenosine	0.83×10^2
Adenosine-Uridine	5.9×10^2

Of course, such data cannot be applied directly to the bonding between nucleotides in the "hydrophobic pocket" of a protein. Above all there are no steric constraints in solution so that base pairings become possible which just do not occur in double stranded nucleic acids. Such studies nevertheless demonstrate that nucleoside interactions are intensified by a hydrophobic environment. Applied to protein biosynthesis this means that the precision of translation of the mRNA nucleotide sequence into the amino acid sequence can be enhanced by an apolar environment at the site of codon-anticodon interaction. It may therefore be expected that nucleotide interactions due to base pairing will not take place on the hydrated surface of the ribosome but in its interior in a hydrophobic environment.

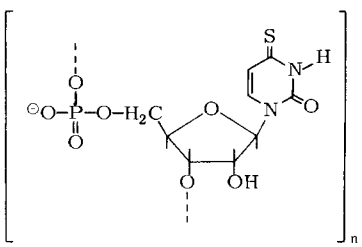
3. Binding of mRNA to the Ribosome. Affinity Labeling

mRNA is bound primarily to the 30S subunit. Several studies have established some connection between the ribosomal protein S1 from this subunit and binding of mRNA. This protein is required for binding of polyuridylic acid [Poly(U)] to ribosomes[19], and conversely Poly(U) protects the protein against degradation by proteases[20]. Poly(U) acts as mRNA and is translated into the protein polyphenylalanine. The protein S1, which can also bind poly(U) in the isolated state[21], is present in only 10 to 30% of ribosomes purified by conventional methods[22]. However, if polysomes are isolated in which all ribosomes are "translationally active", then one molecule of protein S1 is found per ribosome[23]. Protein S1 is necessary for the translation of artificial and natural mRNA[24].

All these findings reveal nothing about which components of the ribosome are actually in the immediate vicinity of the mRNA. We have employed the technique of photoaffinity labeling to identify these components. Affinity labeling provides a means of specifically substituting the active site of an enzyme or a comparable molecule and thus permits its recognition. The biological molecule to be labeled is reacted with a compound Sub-X; Sub is a substrate-like group (or part of a substrate) and X is a reactive group. Owing to the substrate-similarity of Sub, Sub-X is bound to the active center and X (or Sub) can only react with the amino acid chains present there. The aim is to label this side chain with covalently bound X (or Sub) (see Section 6).

In photoaffinity labeling, a substance resembling the natural substrate is bound which reacts with its surroundings on irradiation. Its advantage over conventional affinity labeling is that the duration of reaction between the substrate analog and its environment is precisely defined by the irradiation time.

In our studies we irradiated an analog of Poly(U), poly-4-thiouridylic acid [Poly(s^4U)], in the presence of ribosomes. The naturally occurring 4-thiouracil is one of the "rare bases" in tRNA. On irradiation with 330-nm light the bond between C and S is activated, the S atom oxidized, and the C—S



Poly-4-thiouridylic acid

Poly (s^4U)

bond ruptured by nucleophilic substitution[25]. In the product, side chains of the ribosomal proteins are covalently bonded with the pyrimidine ring. Aliphatic amino groups, *e.g.* the ε-amino group of lysine, can react as nucleophilic groups. Lysine is one of the commonest amino acids in ribosomal proteins[26]. This reaction had already been employed by *Frischauf* and *Scheit* in their studies on DNA-dependent RNA polymerase[27].

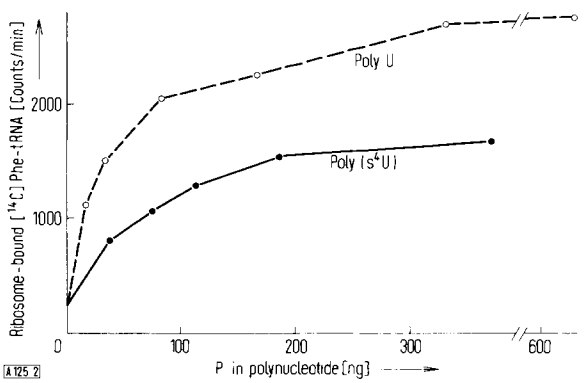


Fig. 2. Binding of [^{14}C]Phe-tRNA to ribosomes in the presence of various amounts of Poly(U) and Poly(s^4U). The [^{14}C]Phe-tRNA was determined by *Leder*'s method [81].

Poly(s^4U), prepared by enzymatic polymerization of 4-thiouridine diphosphate with polynucleotide phosphorylase[28], codes—as shown in Figure 2—like Poly(U) for the binding of phenylalanyl tRNA (Phe-tRNA) to ribosomes and

stimulates the synthesis of polyphenylalanine in the protein-synthesizing system *in vitro*[29]. If complexes of Poly(s^4U), ribosomes, and Phe-tRNA are irradiated with 330-nm light, then polyphenylalanine synthesis is inhibited[30]. Control experiments show that complexes containing Poly(U) instead of Poly(s^4U) as mRNA still synthesize polyphenylalanine in the *in vitro* system after irradiation, indicating that the ribosomes themselves are not inactivated by UV light.

To identify the ribosomal components participating in binding of mRNA, ribosomes incubated with [^{3}H]Poly(s^4U) and Phe-tRNA are irradiated. After digestion of the ribonucleic acids with ribonucleases A and T1 the protein fraction was obtained from the isolated 30S subunits. Electrophoresis on polyacrylamide gels in sodium dodecyl sulfate[31] furnishes a radioactively labeled ribonucleoprotein having a molecular weight of 110000 to 130000 D. Since the molecular weight of the largest ribosomal protein (S1) is only 65000 D it was assumed that the ribonucleoprotein contains several proteins. They were identified by alkaline hydrolysis followed by gel electrophoresis. Most of the radioactivity was found in the protein S1[30]. In addition, radioactivity also appeared in proteins of lower molecular weight. This shows that Poly(s^4U) had reacted with protein S1 and some other proteins. The electrophoretic assignment is confirmed by immunological studies. In this way we could identify the proteins S18 and S21, as well as S1, as components of the ribonucleoprotein complex[32]. Other chemical methods showed that the proteins S1, S18, and S21 are adjacent in the ribosome[33,34]. Identification of the proteins S18 and S21 as components of the mRNA binding site was confirmed by affinity labeling with a derivative of the initiation codon AUG[35].

4. Recognition of the Initiation Site

Apart from the codon AUG or GUG, initiation of protein synthesis requires an additional initiation signal, for AUG codes not only for formylmethionine (fMet) on initiation but also for methionine within the polypeptide chain. Moreover,

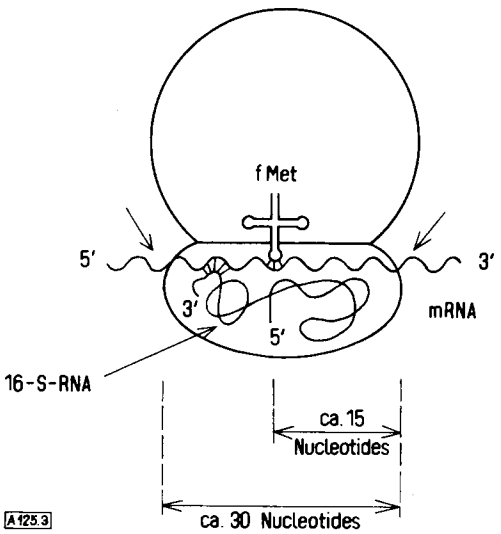


Fig. 3. Scheme for the recognition of the initiation site by the ribosome according to *Shine* and *Dalgarno* [10]. Formation of the initiation complex involves base pairing between a nucleotide sequence at the 3' end of the 16S RNA and a complementary sequence in the mRNA. Furthermore, the initiation codon and the complementary anticodon in fMet-tRNA$_F^{Met}$ also undergo mutual interaction. Since the ribosome protects the bound portion of the mRNA against degradation by ribonuclease, the initiation site of the mRNA can be isolated by treatment with ribonuclease (see Table 2). The arrows indicate the positions of the mRNA up to which ribonuclease cleavage occurs.

Table 2. Complementarity between nucleotide sequences at the 3' end of the 16S RNA from *E. coli* (above) and ribosomal binding sites for natural mRNAs (below). Complementary sequences are underlined. Since the G—C pair is more stable than the A—U pair, the sequences were arranged in such a manner that G—C pairs are preferred. The beginning of the sequence coding for the protein structure is printed in *italics*. The arrows denote those sites in the mRNA ribosome complex at which the mRNA is cleaved by ribonuclease T1 (RNase T1) or ribonuclease A (RNase A). Ribonuclease T1 always attacks after guanine, and ribonuclease A always after pyrimidines (uracil or cytosine).

3'
AUUCCUCCACUAGGUUGGCGUCCm$_2^5$Am$_2^6$AGGGGA$^{5'}$ . . . 16-S-RNA E. coli[36]
HO

RNase T1 RNase T1
5'↓ ↓3'
. . CCUAGGAGGUUUGACCU*AUGCGAGCUUUUAGUG*. . . R17-A-Protein[37]

RNase T1 RNase T1
5'↓ ↓ 3'
. . . AAACAUGAGGAUUACCC*AUGUCGAAGACAACAAAG*. . . R17-Replicase[37]

RNase A RNase A
5'↓ ↓ 3'
. . . AACUAAGGAUGAAAUGC*AUGUCUAAGACAGC*. . . Qß-Replicase[38]

RNase A RNase A
5'↓ ↓ 3'
. . . AGAGCCUCAACCGG$\frac{G}{A}$GUUUGAAGC*AUGGCUUCUAACUUU*. . . R17-Coat protein[37,39,40][a]

RNase T1 RNase T1
5'↓ ↓ 3'
. . . AUAACAAUUUCACAC↑AGGAAACAGCU*AUGACCAUGAUUACG*↓*GAU*. . . Lac-mRNA (*E. coli*)[41]
RNase A RNase A ↑

[a] Two sequences are known for the ribosomal binding site of the mRNA for the R17 coat protein, which differ in one nucleotide (G or A [37, 39]). Replacement of G by A occurs by way of a spontaneous mutation.

whenever a codon ends with A or G and the next codon begins with UG no initiation should occur outside the "reading frame" since it would lead to a protein of no use to the cell.

This initiation signal can only be contained in the nucleotide sequence of the mRNA. In principle, recognition of a sequence in mRNA could arise by interaction with a ribosomal protein or by base pairing with a ribosomal RNA as in codon-anticodon interaction. According to a hypothesis of *Shine* and *Dalgarno*[10] (Fig. 3) the ribosome recognizes the initiation site by base pairing between the nucleotide sequence at the 3′ end of the 16S RNA of the ribosomal 30S subunit and a complementary sequence lying in the vicinity of the initiation triplet. This is illustrated for several examples in Table 2. In the first row the nucleotide sequence of the 3′ end of the 16S RNA is given: the nucleotides responsible for recognition are underlined. They include some nucleotide sequences of the initiation sites of various natural mRNAs. The nucleotides forming the initiation signal are likewise underlined. The sequences are so arranged in the Table that complementary nucleotides appear vertically one below the other. The beginning of the nucleotide sequence coding for the protein is printed in italics. Thus it may be seen that the mRNA for the A protein of phage R17 (a virus attacking *Escherichia coli* and utilizing its translation system for growth) contains the sequence AGGAGGU shortly before the beginning of the information relevant to the structure of the A protein. This sequence is complementary to the UCCUCCA sequence in the 16S RNA and can be bound to it by base pairing.

```
....U C C U C C A....   16-S-RNA
     ‖ ‖‖ ‖ ‖‖ ‖‖ ‖
....A G G A G G U....   R17-A-Protein
```

The other examples in Table 2 demonstrate that this scheme also applies to the initiation sites of other mRNAs, complementarity always obtaining between the initiation signal and nucleotides at the 3′ end of the 16S RNA. The length of the complementary sequence is seven base pairs in the case of the mRNA corresponding to the A protein of R17 phage, and four to five base pairs for the other examples cited. Experimental verification of this hypothesis has recently been reported by *Steitz* and *Jakes*[42]. The differing lengths of the complementary sequences and the associated variation in the affinity of the ribosome for the initiation sites could, together with the secondary structure of the mRNA, determine the frequency of initiation and thus that of translation.

As shown in Section 3, protein S1 is located in the mRNA binding site in the ribosome and, according to the results of other authors, is also bound to the 3′ end of the 16S RNA[43]. Short double-stranded regions of nucleic acids consisting of only four to five base pairs are very unstable in aqueous media, but could be stabilized by a hydrophobic environment (see Section 2). Thus it appears very likely that protein S1 stabilizes interactions between the 3′ end of the 16S RNA and the initiation sequence of the mRNA by acting as a "hydrophobic pocket", and thereby contributes to recognition of the initiation sites in the mRNA.

5. Codon-Anticodon Interaction on Initiation

The ribosomal site at which codon-anticodon interaction takes place (donor site, see Fig. 1) can most readily be located with the aid of the mRNA. Experiments with radioactive Poly(U) have shown that the ribosome protects a section of mRNA some 30 nucleotides long against degradation by ribonuclease A[44]. Using mRNAs of known sequence permitted determination of the distance between the donor site and the entering and leaving sites of mRNA on the ribosome. Since the direction of movement of the ribosome during translation is from the 5′ end to the 3′ end of the mRNA, the leaving and entering sites of the mRNA on the ribosome correspond respectively to the 5′ and 3′ end of the ribonuclease-resistant mRNA fragment (Figs. 1 and 3).

Comparison of the ribosomal binding sites for natural mRNAs in Table 2 reveals that cleavage by ribonucleases always occurs at or directly after the fifth codon of the sequence coding for the protein structure. (The exact position of cleavage will of course also depend upon the specificity of the ribonuclease since ribonuclease A only attacks after U and C, and ribonuclease T1 only after G.) This result was obtained both by nucleotide sequence determination[34-41], and by *in vitro* translation of the fragment of R17 coat protein gene obtained[45,46]. On the basis of these data it is possible to estimate the distances in the ribosome. The distance between two nucleotides in a polynucleotide is 3.4 Å in the stacked form, and 7 Å in the extended form[45]. Given 15 nucleotides between the donor site and the point of entry of mRNA in the ribosome, the distance corresponds to 50 to 100 Å. The diameter of the ribosome is about 200 Å. Assuming the overall length of polynucleotide enclosed in the ribosome to be about 30 nucleotides[44], then the donor site will lie approximately in the middle.

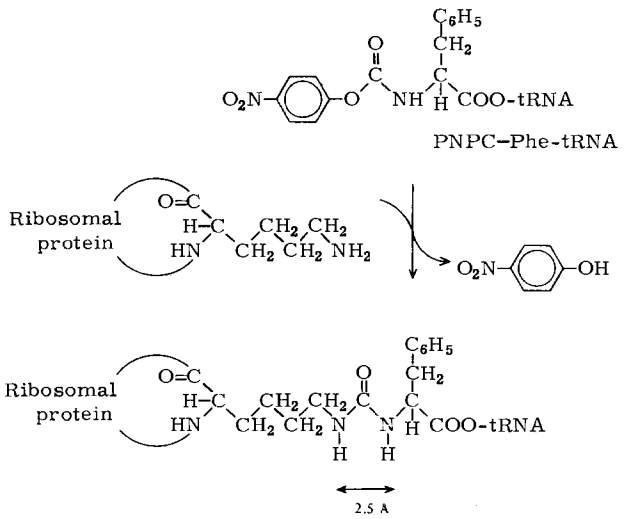
6. The Peptidyl Transferase Site

There are apparently two sites in amino acyl tRNA for interaction with the ribosome: the TΨC region which interacts with a complementary nucleotide sequence in the 5S RNA of the 50S subunit[7], and the amino acylated CCA terminus, which can even be bound by the 50S subunit in isolated form as an amino acylated oligonucleotide fragment[47]. The bound fragment can participate in the peptidyl transferase reaction, showing that it is bound to the correct site in the ribosome. We employ the expression peptidyl transferase center for this catalytic center of the ribosome, initially without distinguishing between the donor and acceptor site.

In order to identify the components of the peptidyl transferase center we resorted once more to the technique of affinity labeling (see Section 3). *Bruton* and *Hartley*[48] proposed the use of the *N*-(*p*-nitrophenoxycarbonyl) derivative of the amino acyl tRNA for affinity labeling of amino acyl tRNA ligases. The *p*-nitrophenoxycarbonyl group (PNPC group) contains an activated ester bond which can be cleaved by nucleophilic substitution, with *p*-nitrophenol acting as leaving group.

Once again the ε-amino group is the principal contender as nucleophilic reactant[49]. Reaction with amino groups of nucleoside bases is improbable owing to the low basicity of such groups.

For conversion into the reagent, Phe-tRNA bearing a [^{3}H]label in the phenylalanine group was treated with *p*-nitrophenyl chloroformate under conditions which only permit reaction at the amino group of the phenylalanyl residue. The resulting *N*-(*p*-nitrophenoxycarbonyl)-phenylalanyl-tRNA



was subsequently incubated with 20 mmol Mg^{2+} per liter and with ribosomes in the presence of Poly(U). After dissociation of the 70S ribosome and centrifugation the radioactivity was found exclusively in the 50S subunit. The radioactively labeled 50S subunits were denatured and the RNA degraded by treatment with ribonucleases A and T1.

The labeled proteins were identified by two-dimensional gel electrophoresis according to *Kaltschmidt* and *Wittmann*[2] and by immunological methods[50]. Most of the reactivity was found in protein L27, less in protein L15, and small amounts in proteins L2 and L16[51].

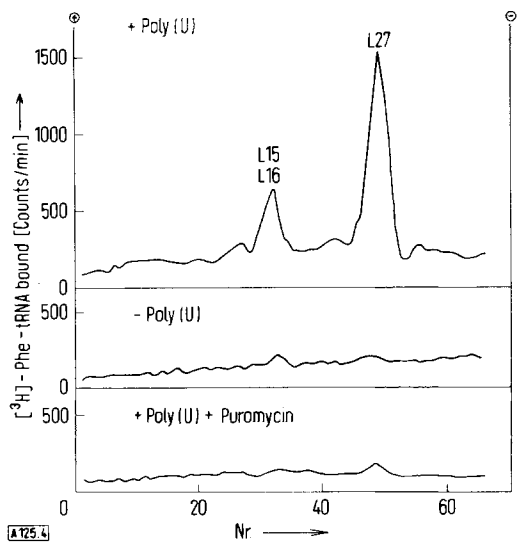


Fig. 4. Affinity labeling of the ribosomal peptidyl transferase site with PNPC-[^{3}H]Phe-tRNA. The reaction only occurs in the presence of Poly(U) and is inhibited by puromycin. The method of *Czernilofsky et al.* [51, 82] was adopted for incubation, for separation of the labeled proteins by one-dimensional polyacrylamide gel electrophoresis, and for identification of the proteins.

Figure 4 shows the results of one-dimensional electrophoresis of isolated L proteins. The radioactivity appears in two bands, corresponding essentially to proteins L15+L16, and L27. It is seen from this Figure that [^{3}H]Phe-tRNA is bound to ribosomal protein only in the presence of Poly(U). Binding of the tRNA derivative is inhibited by puromycin, which reacts with the amino acyl tRNA bound to the donor site to form amino acyl puromycin with release of the amino acid from the ribosome[1]. Thus it is demonstrated that the major proportion of the PNPC-Phe-tRNA reacts with the donor site of the ribosome, from which we deduce that the modified CCA terminus of the PNPC-Phe-tRNA enters into reaction with the peptidyl transferase center of the ribosome. However, since the *N*-acylated Phe-tRNA can be bound both to the donor and to the acceptor site, it cannot be ruled out that a slight amount of PNPC-Phe-tRNA has actually reacted with the acceptor site.

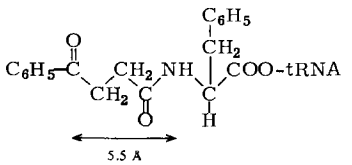
In order to distinguish between the proteins of the donor and the acceptor site we employed a system containing R17 RNA as mRNA together with purified initiation factors, GTP, and the PNPC derivative of the initiator tRNA Met-$tRNA_F^{Met}$ in the presence of 5 mmol of Mg^{2+} per liter. Under these conditions the initiator tRNA is bound exclusively to the donor site[52]. Since the specificity of binding is determined by the $tRNA_F^{Met}$ structure and the initiation factor IF2, we may expect that it is retained for the PNPC-Met-$tRNA_F^{Met}$ derivative. In the ribosomal complex, PNPC-[^{35}S]Met-$tRNA_F^{Met}$ reacts primarily with protein L27 and to a slight extent with protein L15[52]. The reaction was dependent upon the presence of initiation factors and R17 RNA. Hence proteins L27 and L15 are situated at the donor site.

Presumably the CCA ends of the two participating tRNAs come into close spatial proximity during the peptidyl transferase reaction. Since peptidyl transfer proceeds in only one direction, *i.e.* from the donor to the acceptor site, we have to assume that this directional dependence is a manifestation of structural differences between the binding sites for the CCA ends of the two tRNAs. Thus it appears most likely that different proteins are labeled on reaction at the donor and acceptor sites.

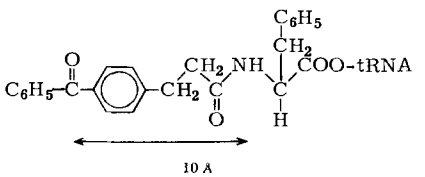
Other authors have used *N*-(bromoacetyl)amino acyl tRNA for affinity labeling, and labeled proteins L27 and L2 from the donor site[53, 54]. The labeling of L27 accords with our own results, but qualitative differences are apparent in the case of L2. Such deviations are to be expected, however, because the PNPC group reacts preferentially with amino groups[49], while bromoacetyl displays a proclivity for reaction with mercapto groups[53]. Protein L16 is the binding protein for the antibiotic chloramphenicol, as demonstrated by reconstitution experiments[55] and labeling studies with the analogous compound iodamphenicol[56]. Chloramphenicol is bound to the acceptor site, and protein L16 should therefore have been labeled from the acceptor site. This agrees with our findings: L16 is labeled only by PNPC-Phe-tRNA but not with PNPC-Met-$tRNA_F^{Met}$, which is specific for the donor site[51, 52]. The labeling of L16 is further enhanced if the conditions are chosen such that the bromoacetyl-Phe-tRNA binds preferentially to the acceptor site[57]. In these studies aromatic azides such as 4-(4-azido-2-nitrophenoxy)phenylacetyl and *N*-(4-azido-2-nitrophenyl)glycyl derivatives of amino acyl tRNAs substituted at the amino acyl NH_2 group were also used. After photoactivation a covalent bond was found at proteins L11 and L18[58]. Protein L11 has been considered as a candidate for peptidyl transferase[59–61]. Proteins L18 and L25 form a complex with 5S RNA which is bound to the 23S RNA *via* protein L5[62].

23S RNA appears to participate directly in the structure of the peptidyl transferase center. Pertinent evidence comes from photoaffinity labeling experiments with *N*-(diazomalonyl)-Phe-tRNA[63], with azido aryl derivatives such as *N*-(4-azido-2-nitrobenzoyl)-Phe-tRNA[64] and *p*-azido-*N*-(*tert*-

butoxycarbonyl)phenylalanyl-Phe-tRNA[65], and with arylcarbonyl derivatives such as 3-benzoylpropionyl-Phe-tRNA (BP-Phe-tRNA) and 3-(4-benzoylphenyl)propionyl-Phe-tRNA (BPP-Phe-tRNA)[66]. We have concerned ourselves with the last-named compound. The carbonyl groups are incorporated in the form of hydroxyl groups into the ribosomal protein to be labeled.

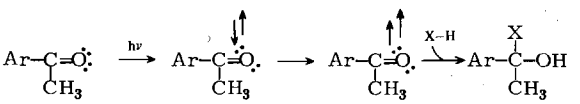


BP-Phe-tRNA



BPP-Phe-tRNA

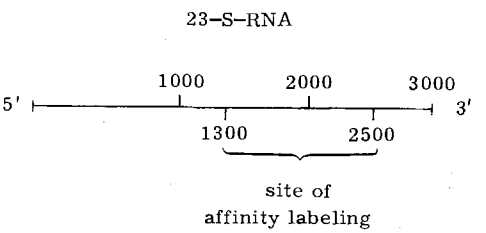
The carbonyl group of aromatic ketones can be excited into a triplet state by UV light of wavelength 320 nm. The excitation energy is *ca.* 70 kcal/mol, roughly corresponding to the dissociation energy of an easily broken C—H bond (dissociation energy for expulsion of a hydrogen atom from the methyl group of toluene: 77 kcal/mol), and is thus considerably lower than the energy required for dissociation of the O—H bond in water, *i.e.* 117.5 kcal/mol[67-69]. Aromatic ketones are therefore particularly suitable for photoaffinity labeling in aqueous systems because no losses can occur by reaction with H_2O. Arylcarbonyl derivatives of amino acyl tRNAs should accordingly give higher yields on photoaffinity labeling of ribosomes than are usually obtained by that technique. Model reactions have shown that acetophenone and benzophenone react with both peptides[69] and nucleosides[70] on photoactivation. Hence aromatic ketones possess the additional advantage of low specificity.



After complex formation between ribosomes, BP- or BPP-[^{3}H]Phe-tRNA, and Poly(U) as mRNA, followed by irradiation, the radioactivity of the 50S subunit was found exclusively in 23S RNA. The significance of this result is underscored by the fact that the distances between the reactive carbonyl group and the amino acyl group of the tRNA differ widely in the two derivatives (5.5 and 10 Å, respectively): labeling of the 23S RNA therefore cannot merely be the result of an accidentally favorable steric arrangement.

After photoaffinity labeling the ribosome still showed peptidyl transferase activity. If a ribosomal complex with Poly(U) and non-radioactively labeled BPP-Phe-tRNA is first irradiated to form the covalent bond between 23S RNA and BPP-Phe-tRNA, and then incubated with [^{3}H]Phe-tRNA, the [^{3}H]radioactivity is likewise bound covalently to 23S RNA. Since the sample contained no radioactivity at the time of irradiation, the [^{3}H]Phe can only have been bound to the 23S RNA by formation of a peptide bond with the covalently linked BPP-Phe-tRNA. However, this is possible only if the photoaffinity reaction between BPP-Phe-tRNA and 23S RNA has taken place at the donor site because no peptidyl transferase reaction could otherwise occur with [^{3}H]Phe-tRNA[70].

Use of suitable degradation methods permits determination of the approximate labeling position in the 23S RNA molecule. 23S RNA consists of about 3000 nucleotides. After partial digestion with ribonucleases, fragments can be isolated which embrace the 1300 nucleotides of the 5′ end and the 500 nucleotides of the 3′ end. These fragments were not labeled. On the other hand, an 18S fragment representing the 23S RNA from nucleotide 1300 to the 3′ end contained the entire radioactivity. Hence it may be concluded that the covalent bond is formed at a position between the bases 1300 and 2500[66].



As can be seen, the peptidyl transferase center is of complex structure. Even on exclusive formation of the derivatized amino acyl tRNA at the donor site, a variety of proteins and 23S RNA are labeled. In this context, particular importance attends the affinity labeling experiments with photoactivatable groups of low specificity such as diazomalonic acid, aromatic azides, and aromatic ketones, which all indicate 23S RNA to be a component of the donor site[63-66]. However, it was also shown by protein labeling that covalently bound amino acyl tRNA is still capable of the peptidyl transferase reaction, thus proving that proteins also belong to the donor site. Hence it may be concluded that the amino acyl group of the tRNA does not have to occupy a particular position in the donor site for the peptidyl transferase reaction to occur. This suggests a certain degree of flexibility in the peptidyl transferase center. On the other hand, it can hardly be imagined that there should not be a preferred binding site guaranteeing maximum rate and efficiency of the amino acyl transfer. 23S RNA might contain such a binding site to which the CCA end of the tRNA is linked by interaction with complementary bases. Confirmation of this hypothesis will have to await sequence analysis of 23S RNA at the position of reaction with BPP-Phe-tRNA.

7. Conclusion and Outlook

An understanding of the processes involved in protein biosynthesis is dependent upon a knowledge of ribosome structure. Precisely this field has undergone important advances[79] during the past few years through the introduction of crosslinking reagents[71,72], the perfection of reconstitution methods[73,74], and electron microscope studies on ribosome dimers linked by antibodies[75-78]. Attempts have already been made to calculate three-dimensional models of the 30S subunit from these results[80].

Affinity labeling permits investigation of the binding sites for natural substrates and thus constitutes an important addition to the other techniques. Moreover, a kind of cinematographic record of a reaction can be obtained with the aid of photoaffinity labeling. This technique opens up new possibilities, especially for systems where the ribosomes carry out processes involving motion.

Although our knowledge of the processes taking place in ribosomes has been greatly extended by the intensive studies of recent years, we still cannot completely describe the mechanism of protein synthesis on a molecular level. However, the methodological armamentarium is now available for obtaining a picture of the ribosome which not only reproduces the steric arrangement of the proteins and nucleic acids but also permits a detailed understanding of protein synthesis.

I am indebted to many friends and colleagues at this institute and other research establishments for discussions, criticism, and valuable stimulation. Particular mention should be made of the fruitful cooperation with Dr. G. Stöffler, Max-Planck-Institut für Molekulare Genetik, Berlin, and Dr. K. H. Scheit, Max-Planck-Institut für Biophysikalische Chemie, Göttingen. Thanks are also due to Prof. Dr. H. Tuppy and my colleagues at the Institut für Biochemie, Vienna, for critical perusal of the manuscript. Financial support by the Fonds zur Förderung der wissenschaftlichen Forschung is gratefully acknowledged.

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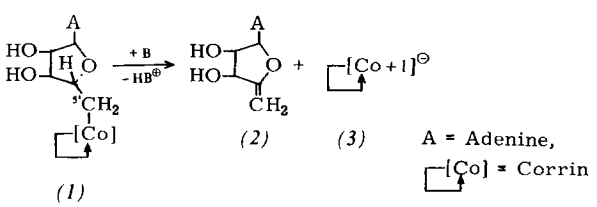
COMMUNICATIONS

Detection of 4',5'-Anhydroadenosine as the Cleavage Product of Coenzyme B_{12} in Functional Holoenzymes[**]

By *R. N. Katz*, *T. M. Vickrey*, and *G. N. Schrauzer*[*]

Coenzyme B_{12} (5'-deoxyadenosylcobalamin) *(1)* undergoes Co—C bond cleavage on reaction with bases to yield 4',5'-anhydroadenosine *(2)* and the nucleophilic Co(I)-corrin derivative *(3)* (vitamin B_{12s}). A reaction of this type was proposed as a possible mechanism of enzymatic coenzyme B_{12} activation, as it generates the highly reactive Co(I)-corrin nucleophile *(3)* from *(1)* in the absence of an external reducing agent[1].



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

Initial experiments with ^{14}C-labeled *(1)* and ethanolamine deaminase revealed the presence of *(2)* in the reacting functional holoenzyme[2]. The presence of enzyme-bound *(3)* is indicated by the inactivating effect of N_2O, a mild oxidizing agent which acts as a selective oxidant of Co(I)-nucleophiles.

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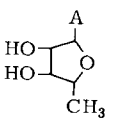
To obtain further support for our concept of the mechanism of enzymatic coenzyme B_{12} activation, we have since performed similar experiments with D,L-propanediol hydrolase (dioldehydrase), this time with 5'-^3H-labeled coenzyme B_{12}. Commercially available enzyme from Pierell, S.p.A. (Milan, Italy), was incubated with ^3H-labeled coenzyme under argon at 25°C in the dark. After 15—30 min, the incubates were lyophilized in the dark. The solid residues were treated with 0.5 ml of CH_3OH and authentic unlabeled *(2)*, as well as 5'-deoxyadenosine *(4)*, were added. Drops of the methanolic solutions were spotted on Whatman No. 1 paper strips and



(4)

chromatographed in the dark, using water-saturated 2-butanol as the ascending phase, or on silica gel plates with ethyl acetate/methanol (6:1) as the eluent. The presence of ^3H-labeled *(2)* and of *(4)* was ascertained by measurement of the ^3H-radioactivity profiles and comparison of the R_f-values[3]. A typical activity profile, which demonstrates the presence of *(2)* and possibly of traces of *(4)*, is shown in Figure 1.

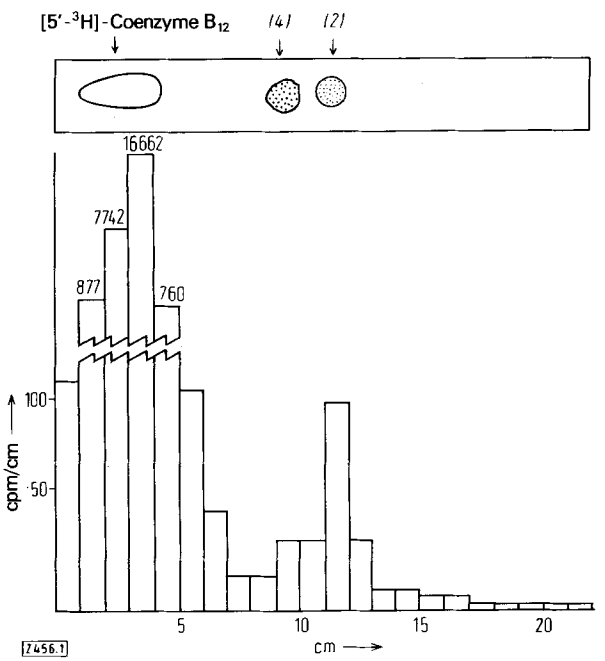


Fig. 1. Radioactivity profile of a paper chromatogram (Whatman No. 1) of the freeze-dried residue of a reacting solution of D,L-propanediol hydrolase incubated with 5'-^3H-labeled coenzyme B_{12} and D,L-propanediol as the substrate. The contours of the spots of *(2)* and *(4)*, which both were added prior to chromatography (ascending phase: water-saturated 2-butanol), were visualized under UV light and by exposure to I_2 vapor. ^3H-radioactivity was mainly present in the spot consisting of authentic *(2)*.

The identity of *(2)* was ascertained by spraying the chromatograms with a 1% solution of $KMnO_4$ in 2% aqueous sodium carbonate. This reagent is relatively unreactive towards *(4)*, but rapidly oxidizes *(2)* at the olefinic double bond[4]. This reaction was accompanied by a loss of ^3H-radioactivity in the respective spot to 38% of the original value. Compound *(4)* was occasionally observed in larger amounts than in Figure 1, but was often also not detected at all. Since *(1)* undergoes reductive Co—C bond cleavage to yield *(4)*[5], we consider it as a by-product of a side-reaction unrelated to the process of enzymatic catalysis.

Compound *(2)* was detectable only if the incubations were performed with exclusion of oxygen and mild methods of work-up, such as lyophilization at −78 °C (dry ice/acetone), and with active enzyme preparations[6].

Analogous experiments with purified ethanolamine ammonia lyase produced similar results; a radioactivity profile of a chromatography strip is shown in Figure 2.

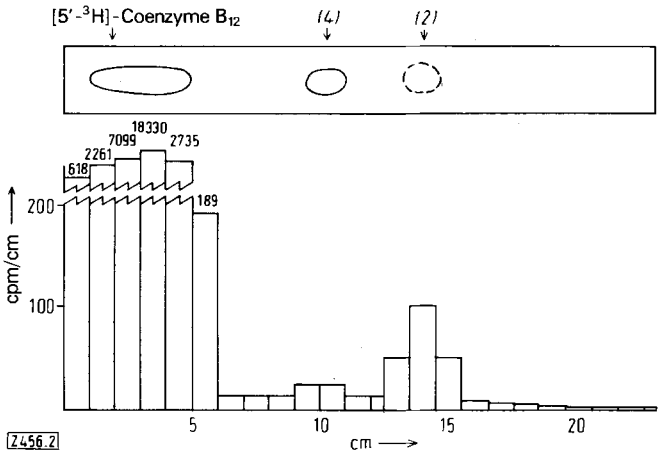


Fig. 2. Radioactivity profile of a paper chromatogram (Whatman No. 1) of the freeze-dried residue of a reacting solution of ethanolamine deaminase incubated with 5'-^{3}H-labeled coenzyme B_{12} (reaction conditions as outlined in Refs. [2] and [6]).

The detection of *(2)* in two coenzyme B_{12}-dependent enzymes supports our concept according to which *(1)* is enzymatically activated by Co—C-bond *heterolysis* rather than homolysis and that the highly nucleophilic Co(I)-derivative of the corrinoid cofactor is the catalytically active species.

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(1), 13870-90-1; *(2)*, 20535-04-0; *(3)*, 18534-66-2; *(4)*, 4754-39-6

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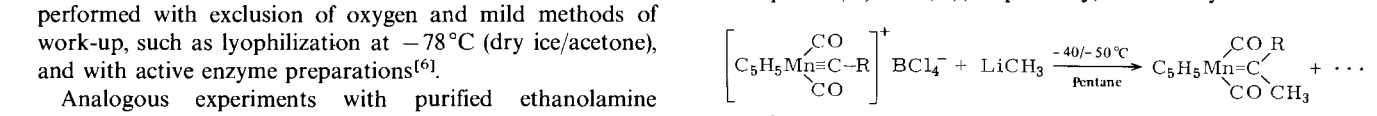
[6] The experiments were performed in Pyrex centrifuge tubes of 15 ml capacity which were rubber-serum-capped, flushed with pure argon for 20 min, and covered with aluminum foil for protection against light. One vial of the commercial enzyme (29 mg, 7.0 units) was dissolved in 7.0 ml of 0.01 M potassium phosphate buffer (pH 7.4) containing 2% v/v of D,L-propanediol. As a rule, 0.9 ml of enzyme stock solution was injected into the centrifuge tubes and the reaction was initiated by the addition of 0.1 ml of a solution containing 12.6 nmoles of coenzyme B_{12}. The ^{3}H-activity of the coenzyme solution added was 11.3 nC (25000 cpm).

Dimethylcarbene- and Methylphenylcarbenedicarbonyl(η-cyclopentadienyl)manganese[1]

By *Ernst Otto Fischer, Roger Lee Clough, Gerhard Besl*, and *Fritz Roland Kreissl*[*]

The novel manganese compounds *(1)* and *(2)* are the first transition metal-carbene complexes in which a dialkyl or an alkylarylcarbene is stabilized as ligand to a metal atom, in this case manganese. Diarylcarbene complexes of the same system have already been reported[2].

(1) and *(2)* are formed on reaction of the cationic carbyne complexes *(3)* and *(4)*, respectively, with methyllithium:

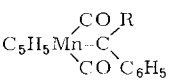


(3), R = CH_3
(4), R = C_6H_5

(1), R = CH_3
(2), R = C_6H_5

The red, crystalline products are readily soluble in organic solvents. Their composition and structure follows from elemental analysis and spectroscopic investigations.

In each case the IR spectra (in *n*-hexane) show two intense bands in the ν_{CO} region. Their shift to higher wave numbers compared to the analogous phenylmethoxycarbene complex *(6)*[3] supports the assumption of stronger back-bonding from metal to carbene carbon.



(5), R = C_6H_5
(6), R = OCH_3

IR: ν_{CO} absorption [cm^{-1}]

(1)	*(2)*	*(5)* [2]	*(6)* [3,4]
1974	1980	1977	1960
1910	1918	1919	1897

The ^{1}H-NMR spectrum of *(1)* contains two sharp peaks at δ = 5.07 (C_5H_5) and 3.02 ppm (CH_3) in the intensity ratio 5:6 (in [D_6]-acetone, relative to CD_2HCOCD_3 = 2.03 ppm). *(2)* shows a multiplet at 7.2 ppm (C_6H_5) and two singlets, one at 4.75 (C_5H_5) and one at 3.15 ppm (CH_3) (intensity ratio: 5:5:3 recorded in $CDCl_3$, rel. to TMS int.).—In the ^{13}C-NMR spectrum the signal of the carbene carbon of *(1)* and of *(2)* appears at much lower field than that of *(6)*.

^{13}C-NMR shifts [ppm], recorded at −55 °C in [D_6]-acetone, rel. to CD_3COCD_3 = 206.5 ppm.

	δC-carbene	δCO	δC_6H_5	δC_5H_5	δCH_3
(1)	372.75	233.36	—	89.99	52.29
(2)	363.69	232.92	167.01 127.31 125.26 118.90	90.63	68.41
(6)	334.76	233.24	156.43 128.06 127.73 123.42	88.36	63.87

The mass spectra contain the molecular ion peaks at m/e = 218 [*(1)*] and 280 [*(2)*], respectively, as well as peaks

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due to fragments after successive loss of two CO groups, the carbene residue, and the C_5H_5 ligand.

Experimental:

All work is carried out in anhydrous and oxygen-free solvents under N_2.

Dicarbonyl(η-cyclopentadienyl)methylcarbynemanganese tetrachloroborate (3): BCl_3 is added to a stirred solution of $C_5H_5Mn(CO)_2C[CH_3(OCH_3)]$[3] (1.76 g, 7.5 mmol) in pentane (100 ml) at −40 °C. The precipitate which is formed is filtered off, washed several times with pentane, and dried in a high vacuum. For further purification the substance is dissolved in CH_2Cl_2 and covered with pentane. After drying, analytically pure *(3)* is obtained in the form of a finely crystalline, yellow-orange thermolabile powder. Yield 2.16 g (80.7 %).

Dicarbonyl(η-cyclopentadienyl)dimethylcarbenemanganese (1): To a suspension of *(3)* (1.94 g, 5.45 mmol) in pentane (50 ml) at −40 °C is added a suspension of $LiCH_3$ (120 mg, 5.45 mmol) in the same amount of the same solvent. After 3 hours' stirring at −40 °C the red solution is separated from the solid components of the reaction mixture, concentrated to 50 ml, and chromatographed on a silica gel column at −25 °C with pentane. Of the three zones which are formed the middle (red) one contains the desired product. After removal of solvent and recrystallization, *(1)* is obtained as dark red crystals which melt below room temperature. Yield: 220 mg (18.5 %).

Dicarbonyl(η-cyclopentadienyl)methylphenylcarbenemanganese (2): To a suspension of *(4)*[4] (3.1 g, 7 mmol) [preparation analogous to that of *(3)*] in pentane (20 ml) is added a solution of $LiCH_3$ (10.5 mmol) in ether. The mixture is stirred for 7 h at −50 °C. After removal of solvent the residue is chromatographed on silica gel at −40 °C, first with pentane and later with pentane/ether. After two recrystallizations from pentane, *(2)* is obtained as red crystals, m. p. 35—36 °C. Yield: 260 mg (14 %).

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(1), 59831-13-9; *(2)*, 59831-14-0; *(3)*, 59831-16-2; *(4)*, 59831-18-4; *(6)*, 12245-61-3; $LiCH_3$, 917-54-4; $C_5H_5Mn(CO)_2C[CH_3(OCH_3)]$, 12244-94-9

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Intercalation Compounds of Zirconium Phosphate

By *Dietmar Behrendt*, *Klaus Beneke*, and *Gerhard Lagaly*[*]

The ability of layer compounds to form intercalation compounds requires a particular kind of structure and bonding between the layers. Apart from graphite only few inorganic layer compounds capable of intercalating neutral molecules between the layers were hitherto known: kaolinite[1]; binary sulfides like TiS_2 and TaS_2[2]; and crystalline silicic acids[3].

We have now found that crystalline M^{IV} phosphates $M(HXO_4)_2 \cdot nH_2O$, with M = Zr, Si, Sn, Ce and X = P, As take up certain neutral molecules to form a large number of intercalation compounds. Zirconium phosphate $Zr(HPO_4)_2 \cdot nH_2O$ ($n = 0, 1, 2$) may be cited as an example. The layer structure of the monohydrate was established by *Clearfield*[4] and confirmed with the aid of cation exchange experiments with *n*-alkylammonium ions by *Michel* and *Weiss*[5].

All three hydrates can be used for formation of intercalation compounds. For this purpose the zirconium phosphates are allowed to react for several days at 60—80 °C with the corresponding liquids, and in the case of solid guest compounds with an excess of a concentrated aqueous solution. $Zr(HPO_4)_2 \cdot 2H_2O$ (γ-ZrP according to ref. [4]) reacts with a larger number of guest molecules than the monohydrate (α-ZrP) because the zirconium phosphate layers are widely separated from each other by bimolecular water layers. γ-ZrP also reacts with long-chain compounds (*e.g.* hexanol : basal spacing : 24.9 Å; butyronitrile : 21.3 Å). The intercalation compounds of $Zr(HPO_4)_2$ (β-ZrP) are identical with those of γ-ZrP provided they are not prepared with exclusion of water because β-ZrP immediately transforms into γ-ZrP in the presence of H_2O.

The basal spacings of the intercalation compounds of α-ZrP and γ-ZrP are different (Table 1). In α-ZrP they repeatedly suggest that the H_2O molecules are replaced by approximately

Table 1. Basal spacings d_L of the intercalation compounds of $Zr(HPO_4)_2 \cdot H_2O$ (α-ZrP) and $Zr(HPO_4)_2 \cdot 2H_2O$ (γ-ZrP).

	Intercalated molecule	Basal spacing d_L [Å] α-ZrP	γ-ZrP
		7.6	12.3
(1)	Dimethyl sulfoxide	10.8	16.2
(2)	*N*-Methylformamide	10.5	15.9
(3)	*N,N*-Dimethylformamide	11.2	15.8
(4)	Urea [a]	9.4	13.6
(5)	*N,N*-Dimethylurea [a]	10.6	14.1
(6)	*N,N'*-Dimethylurea [a]	9.4	15.9
(7)	Hydrazine hydrate	9.4	14.6
(8)	Piperidine	13.4	17.8

[a] Concentrated aqueous solution.

spherical guest molecules (Table 2). The increase in basal spacing Δd_L is then equal to the diameter of the intercalated molecule *D* minus 2.8 Å (diameter of a water molecule). Of course, this cannot hold if the intercalated molecule is unable to adopt a spherical shape, as in the case of piperidine. Urea compounds warrant interest; only the unsymmetrical methyl derivative *(5)* appears to assume a spherical shape.

The intercalation compounds of α-ZrP are characterized by their remarkable stability. The guest molecules are retained so firmly between the layers that their removal is difficult even *in vacuo* above 100 °C. The monohydrate itself displays similar stability.

Many guest molecules in γ-ZrP replace only one H_2O molecule; the increase in basal spacing is then equal to or slightly greater than *D* minus 2.8 Å. In some cases (urea, *N,N*-dimethylurea, glycol, glycerol) both H_2O molecules are replaced by an intercalated molecule (Δd_L significantly smaller than *D* minus 2.8 Å).

The reaction of α-ZrP and γ-ZrP with alkylamines[6] to form compounds with large basal spacings (*e.g.* α-ZrP + hexylamine : 23.3 Å; + dodecylamine : 36.4 Å) is also an intercalation reaction. However, the alkylamines are bound with formation of alkylammonium ions and unlike the other intercalated compounds cannot be washed out.

Zirconium phosphate has a number of superior properties compared with other intercalating compounds: apart from their ability to intercalate neutral molecules between the layers, their protons have been known for some time to be susceptible to cation exchange reactions in the normal pH range, in

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Table 2. Interpretation of the intercalation compounds of α-ZrP and γ-ZrP. d_L is the basal spacing of the intercalation compound and D is the diameter of the intercalated molecule; the diameter of a water molecule is 2.8 Å.

	Intercalated molecule	α-ZrP Increase in basal spacing $d_L - 7.6$ [Å]	$D - 2.8$ [Å]	γ-ZrP Increase in basal spacing $d_L - 12.3$ [Å]
(1)	Dimethyl sulfoxide	3.2	3.3	3.9
(2)	*N*-Methylformamide	2.9	2.9	3.6
(3)	*N,N*-Dimethylformamide	3.6	3.5	3.5
(7)	Hydrazine hydrate	1.8	1.9	2.3
(4)	Urea	1.8	2.5	1.3
(5)	*N,N*-Dimethylurea	3.0	3.2	1.8
(6)	*N,N'*-Dimethylurea	1.8	3.4	3.6

particular by alkali metal ions[7] and long chain organic cations[5]. Thus zirconium phosphate is capable of undergoing two types of interface reactions which are mutually excluded in the compounds studied hitherto: the clay mineral kaolinite only forms intercalation compounds, whereas the clay mineral montmorillonite has a pronounced cation exchange capacity.

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$Zr(HPO_4)_2 \cdot H_2O$, 13933-56-7; $Zr(HPO_4)_2 \cdot 2H_2O$, 13772-31-1; dimethyl sulfoxide, 67-68-5; *N*-methylformamide, 123-39-7; *N,N*-dimethylformamide, 68-12-2; urea, 57-13-6; *N,N*-dimethylurea, 598-94-7; *N,N'*-dimethylurea, 96-31-1; hydrazine, 302-01-2; piperidine, 110-89-4

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Conformations and N-Inversion Barriers in Tropane Compounds[1]

By *Hans-Jörg Schneider* and *Lothar Sturm*[*]

The focal point of the controversy surrounding the conformation of piperidine is the question whether the lone pair or a substituent such as hydrogen assumes the equatorial position at the nitrogen, which is regarded as being the less hindered[2]. We have attempted to apply ^{13}C-NMR low-temperature spectroscopy to inversion at nitrogen but exchange between equatorial and axial N—H bonds proved to be too fast in the case of piperidine. However, by introducing the C6—C7 bridge it was possible to slow down the inversion to such an extent that two conformers having distinct pairs of signals for all C atoms except C3 appear in the ^{13}C-NMR spectra of the resulting tropane compounds *(1)* at low temperatures. e-*(1)* is the conformer with equatorial *N*-substituent, and a-*(1)* that having axial *N*-substituent (relative to the piperidine system).

The ground state energy difference (Table 1) calculated for *(1a)* from the intensity ratios agrees with the value obtained by ^{1}H-NMR spectroscopy (0.90 kcal/mol) from the split CH_3 signal at −100 °C. While the methyl group accordingly displays a pronounced conformative preference, the ^{13}C-NMR study on nortropane *(1e)* under the same conditions reveals an almost *equal* population of e-*(1e)* and a-*(1e)*. Thus the approximately equal effective interaction magnitude of a lone pair and hydrogen have become experimentally demonstrable for a given molecular geometry.

Assignment of the observed conformations to e-*(1)* and a-*(1)* is based on the shielding due to the *syn*-γ effect of the methyl group[3] which should be up to 6 ppm greater for C2,4 in a-*(1)*, X = CH_3, and C6,7 in e-*(1)*, X = CH_3. The shift effects actually found for the γ-C atoms in e-*(1)* and a-*(1)*, X = CH_3, are about 4 ppm greater, which is attributable to additional shielding by the lone pair in the case of an antiperiplanar arrangement of the C_β—C_γ bond [as in a-*(1)* with regard to C2,4, but not in e-*(1)* with regard to C6,7]. This shielding which has important implications for the shift

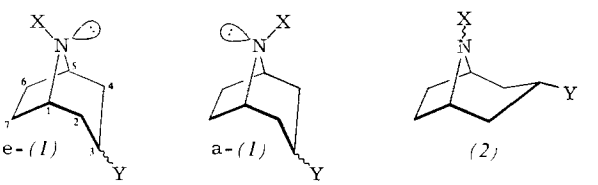

Table 1. ^{13}C-NMR shifts, ground state energy differences (ΔG^0), and inversion barriers (ΔG^*, ΔH^*, ΔS^*) in tropane conformers *(1)*. Shifts are relative to TMS [ppm]. An asterisk signifies interchangeable assignments; the energy parameters (in kcal/mol and cal K^{-1} mol^{-1} respectively) are the best values from measurement of four pairs of signals in each case [three for *(1e)*], the errors given are the mean deviations obtained from regression analysis (without systematic errors). ΔG^* was determined by complete line shape analysis over a range of about 50°.

	X	Y	C1,5		C2,4		C6,7		*N*-CH_3		C3	$\Delta G^0 \cong \Delta H^0$	ΔG^*_{233}	ΔH^*	ΔS^*
			e-*(1)*	a-*(1)*	e-*(1)*	a-*(1)*	e-*(1)*	a-*(1)*	e-*(1)*	a-*(1)*	*(1)*	[e]			
a	CH_3	H [a]	61.85	57.04	32.35	22.15	25.53	28.77	42.10	32.71	16.37	0.91	9.17 ± 0.03	13.2 ± 1.1	+18 ± 5
b	CH_3	*endo*-OH [b]	60.74	56.36	39.50	29.87*	25.34	28.54*	41.13	32.64	63.41	1.20	11.05 ± 0.09	14.3 ± 0.6	+14 ± 3
c	CH_3	*exo*-OH [b]	61.85	58.16	41.58	32.61	26.25	29.17	40.80	32.82	63.08	0.71	11.3 ± 0.3		
d	CH_3	*endo*-CH_3 [a]	61.26	56.65	38.27	28.07*	25.60	28.85*	41.64	33.00	22.48 [c]	0.62	9.26 ± 0.02	12.3 ± 0.5	+14 ± 3
d	CH_3	*endo*-CH_3 [b]	61.59	57.18	37.87	28.41*	25.53	28.68*	40.99	32.70	22.41 [d]	0.99	10.73 ± 0.04	14.7 ± 0.4	+17 ± 2
e	H	H [a]	55.25	53.43	31.59	33.93	30.29	27.95	—	—	17.55	−0.08	7.79 [f] ± 0.02	6.3 ± 0.3	− 9 ± 2

[a] 6% in $CFCl_3$; −100 °C [−133 °C for *(1e)*]. [b] 6% in $CFCl_3/CH_3OH$ (2:1), −70 °C. [c] (C3)-CH_3: 25.40. [d] (C3)-CH_3: 25.53. [e] $\Delta G^0 = \Delta G_{a-(1)} - \Delta G_{e-(1)}$; $\Delta S^0 = 0 \pm 2$. [f] Measured at −100 °C.

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mechanism[4] is reduced on participation of the lone pair in hydrogen bonding (*e.g.* with methanol, Table 1).

Bulky substituents in the *endo*-3-position of tropanes *(1)* can lead to adoption of the boat form *(2)* or to flattening[5] of the chair. The *endo*-3-methyl compound *(1d)* can be prepared by reaction of tropinone with methyllithium, dehydration of the resulting tertiary alcohol, and subsequent hydrogenation. Its existence in the boat form *(2)* can be ruled out in the same way as for tropine *(1b)* on the basis of the ^{13}C-NMR shifts, which in particular for C3 should appear some −7 ppm upfield for *(2)*. In fact the signals of C3 and (C3)-CH_3 recorded above 230 K display a broadening of 1—2 Hz which must be attributed to some slight participation of the boat form *(2)*. The flattening of the piperidine chair reduces hindrance by the axial hydrogen atoms on C2 and C4 and thus shifts the N-invertomer equilibrium in favor of a-*(1)* (see Table 1).

Preliminary measurements confirm the shift of the invertomer equilibrium by protic solvents which is frequently discussed for piperidine. It appears that the conformer having the axial electron pair e-*(1d)* will profit more from hydrogen bonding with methanol than will a-*(1d)*. In the case of the piperidine analog nortropane *(1e)* inversion is so fast in the presence of methanol that not even line broadening can be observed at −100 °C. Line shape analyses with 10, 6, and 2 mol % of nortropane in $CFCl_3$ and with admixture of dimethylformamide indicate an almost constant inversion barrier to within ±0.15 kcal/mol, so that the unexpectedly small activation energy (see Table 1) relative to the *N*-methyl compound cannot be explained by participation of an intermolecular proton exchange but rather in terms of an additional tunneling mechanism[6, 7].

The significantly negative ΔS^* value for nortropane *(1e)* can likewise be regarded as the result of a tunneling contribution decreasing with rising temperature. The increase in activation energy on going from $CFCl_3$ to CH_3OH in the case of *(1b)* is attributable to the desolvation necessary in the inversion transition state in a protic solvent[6].

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(1a), 529-17-9; *(1b)*, 120-29-6; *(1c)*, 135-97-7; *(1d)*, 60118-06-1; *(1e)*, 280-05-7

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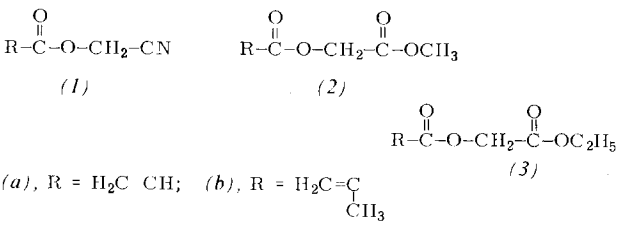
Crosslinked Polymers Having Activated Ester Groups—A Versatile Support Material[**]

By *Hubert Köster* and *Walter Heidmann*[*]

Since the use of a polystyrene crosslinked with 1 to 2 % of divinylbenzene for solid phase synthesis of polypeptides by *Merrifield*[1], variously functionalized polymers have found application in the synthesis of oligomeric natural products, as polymeric reagents, for immobilization of enzymes, and in affinity chromatography. The first two applications mainly utilize inert hydrophobic polymers having a defined functional group, while the last two require hydrophilic polymers.

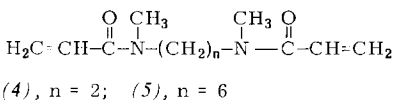
It appeared of interest to develop a single insoluble swellable polymer from which products having different properties can be generated and therefore can be utilized for all four kinds of application. With this aim in mind we have synthesized the acrylic esters *(1a)*, *(2a)*, and *(3a)*, as well as the methacrylic esters *(1b)*, *(2b)*, and *(3b)*[2] and polymerized them in



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

(a), R = H_2C=CH; *(b)*, R = H_2C=C(CH$_3$)

the presence of *N*,*N*′-dimethyl-*N*,*N*′-ethylenebis(acrylamide) *(4)* or *N*,*N*′-dimethyl-*N*,*N*′-hexamethylenebis(acrylamide) *(5)* as crosslinking reagents and of *N*,*N*-dimethylacrylamide to improve the solubility of the crosslinking agent. A non-macroporous bead polymer is obtained. If inert components (*e.g.* 1-heptanol, *n*-butyl acetate, di-*n*-butyl ether) are present during the polymerization step macroporous bead polymers can also be obtained.



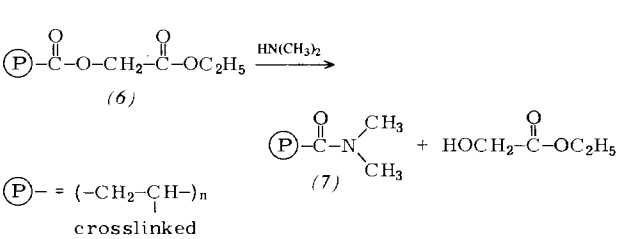
(4), n = 2; *(5)*, n = 6

Polymeric ester (6)

A mixture of ester *(3a)* (17.8 g), *N*,*N*-dimethylacrylamide (1.8 g, 10 wt %), compound *(4)* (0.4 g, 2 wt %), and azoisobutyronitrile (100 mg) was added under N_2 to a stirred (720 rpm) solution of polyvinyl alcohol (3 g) in water (250 ml). After polymerization for 1 h at 60 °C, 2 h at 70 °C, and 2 h at 80 °C the product was washed with hot water, ethanol, acetone, benzene, acetone, ethanol, and ether and dried *in vacuo* at 50 °C. The sieve fraction of 0.1 to 0.315 mm particle diameter was used. Yield of (6): 12.1 g (61 %).

The bead polymers of acrylic esters are soft, and those of methacrylic esters hard and flowable. They have a degree of swelling (volume after solvation relative to volume of dry beads) of 6 in acetone and DMSO, 4 in dimethylformamide and acetonitrile, and 2 in benzene and ethyl acetate.

The activated ester groups in polymer *(6)* provide a means of incorporating other functional groups into the product. Thus reaction of *(6)* with dimethylamine affords the polymeric carboxamide *(7)*. As a result of the excellent miscibility of



(6) *(7)*

Ⓟ = (−CH$_2$−CH(−)−)$_n$ crosslinked

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N,N-dimethylacrylamide with most solvents (*e.g.* water, alcohols, benzene, light petroleum) a bead polymer *(7)* is only accessible in this way.

Polymeric carboxamide (7)

To a suspension of polymer *(6)* (12.1 g) in acetone (350 ml) and glacial acetic acid (600 mg) in a glass autoclave cooled to 0 °C is added anhydrous dimethylamine (100 ml). The mixture was shaken for 30 min at room temperature and 24 h at 50 °C; after washing with acetone, ether, acetone, pyridine, ethanol, acetone, and ether the polymer was dried *in vacuo* at 50 °C. Elemental analysis (N 4.9 %) shows the polymer to contain 34.7 mol % of amide groups. *(7)* possesses excellent solvation properties. The degree of swelling is 12 in pyridine, 15 in dimethyl sulfoxide, 10 in dimethylformamide, 5 in water, 5 in ethanol, and 12 in water/methanol (1 : 1, v/v).

It is also possible to react the activated ester groups in *(6)* first with a limiting amount of a nucleophile (primary reactant) and subsequently with another nucleophile (secondary reactant). In this way the amount of primary reactant to be introduced and the solvation (swelling) properties of its environment can be varied within wide limits. In *(7)* part of the *N,N*-dimethylamide groups obtained on reaction with an excess of dimethylamine can be hydrolyzed to carboxyl groups. A polymer of this kind is used in the solid phase synthesis of oligonucleotides[3].

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(3a), 21045-68-1; *(4)*, 60134-80-7; *(6)*, 60134-81-8; *N,N*-dimethylacrylamide, 2680-03-7; dimethylamine, 124-40-3

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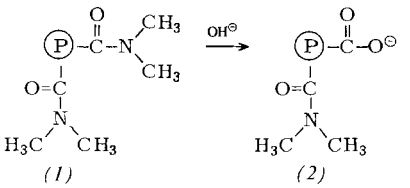
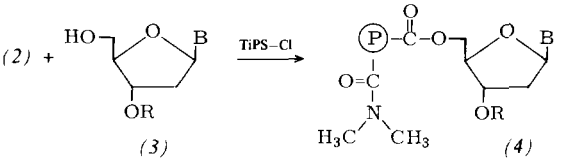
Oligonucleotide Synthesis on a Polymeric Support with Avoidance of Failure Sequences[1][**]

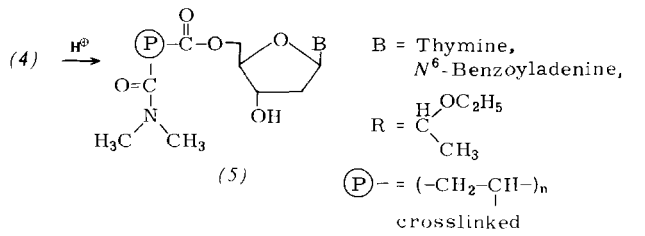
By *Walter Heidmann* and *Hubert Köster*[*]

Using a non-macroporous polystyrene crosslinked with 1 % of divinylbenzene, *Merrifield* and *Gutte*[2] were able to synthesize polypeptide chains having a molecular weight of more than 15000. Since the decanucleotides required for a DNA synthesis have a molecular weight of only *ca.* 5000[3], a weakly crosslinked, non-macroporous polymer should possess cavities of adequate size to permit its functioning as a support for an oligonucleotide synthesis. A disadvantage of this support for synthesis of oligonucleotides using the diester concept has so far consisted in the failure to find satisfactory swelling conditions for the nonpolar polymer bearing polar oligonucleotide chains.

Our previous communication[4] described the synthesis of a support *(1)* devoid of these difficulties. The carboxylate groups in *(2)*, which arise by partial hydrolysis of the amide groups in *(1)*, serve to anchor the first nucleoside *(3)*. It is protected by the acid-labile α-ethoxyethyl group at the 3'-OH group[5]. Esterification is accomplished after activation of the carboxylate groups of *(2)* with 2,4,6-triisopropylbenzenesulfonyl chloride (TiPS—Cl).





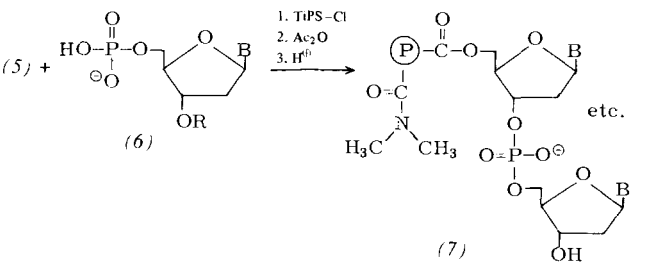


Carrier-bound nucleoside (5)

The support *(2)* (4 g, 1.6 mmol of carboxylate groups) was shaken for 24 h at room temperature in pyridine (50 ml) containing TiPS—Cl (8 mmol). The activated polymer was washed with pyridine and ether in the absence of moisture and shaken with the nucleoside *(3)* (7.2 mmol) in pyridine (20 ml) at room temperature. The unreacted activated carboxylate groups were blocked by 6 hours' shaking with an excess of methanol. The product *(4)* was washed with pyridine and ether and dried *in vacuo*. It contained 85 μmol *(3)*/g, which could be released by treatment with conc. aqueous ammonia for 16 h at room temperature or with 1 N aqueous sodium hydroxide at 0 °C for 30 min. Removal of the α-ethoxyethyl group from the carrier-bound nucleoside *(4)* could be accomplished quantitatively by 15 hours' shaking in glacial acetic acid/water/methanol (3 : 4 : 3, v/v). After thorough washing with pyridine, ethanol/water (1 : 1, v/v), and ether the product *(5)* is dried *in vacuo* at 40 °C.

Carrier-bound dinucleotide (7)

The support *(5)* (1 g, 85 μmol of bound nucleoside) is shaken in pyridine (10 ml) with the nucleotide *(6)* (4 mmol) and TiPS—Cl (8 mmol) for 8 h. Washing with pyridine is followed by drying *in vacuo*. The product is shaken for 16 h with acetic anhydride/pyridine (1 : 1, v/v, 10 ml) at room temperature, washed with pyridine and ether, and the α-ethoxyethyl group then removed. After washing and drying of *(7)* the nucleotide chain can once again be elongated.



Use of an alkali-labile anchoring and an acid-labile 3'-*O* protecting group permits blocking of those 3'-OH groups which have failed to react in a condensation reaction by acylation, thus avoiding failure sequences. Furthermore using

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this strategy, the heterocyclic bases remain fully acylated prior to each condensation. Since removal from the carrier is feasible under conditions not affecting the *N*-acyl groups the trunk sequences can be re-used after chromatographic separation.

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CAS Registry numbers:
(3a), R = thymine, 60134-98-7; *(3b)*, R = N^6-benzoyladenine, 60134-99-8

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[2] *B. Gutte* and *R. B. Merrifield*, J. Am. Chem. Soc. *91*, 501 (1969).
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[4] *H. Köster* and *W. Heidmann*, Angew. Chem. *88*, 576 (1976); Angew. Chem. Int. Ed. Engl. *15*, 546 (1976).
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Hydrophobic Interactions between Metal Complexes of Aromatic Ligands and 3-(Trimethylsilyl)-1-propanesulfonate and Their ^{1}H-NMR Spectroscopic Detection[**]

By *Paul R. Mitchell* and *Helmut Sigel*[*]

Although tetramethylsilane has been almost universally accepted as the reference standard for proton NMR in non-aqueous solutions, various reference compounds have been used in aqueous solutions including acetonitrile, dioxane, *tert*-butanol, and the tetramethylammonium, 3-(trimethylsilyl)propionate *(2)*, and 3-(trimethylsilyl)-1-propanesulfonate ("DSS") ions *(1)*. With high concentrations of aromatic solutes[1] hydrophobic interactions involving trimethylsilyl groups[2] may influence the NMR spectrum; however, such concentrations are not normally used for routine NMR work. Micelle formation, which also has an effect, only occurs at very high concentrations of the trimethylsilyl compound[3], which may also act as a surfactant[4].

However, when $(CH_3)_3Si[CH_2]_3SO_3^{\ominus}$ *(1)* was used as a reference in an investigation of the NMR spectrum of metal complexes, anomalous chemical shifts were observed in the presence of $[Zn(phen)]^{2+}$ or of $[Zn(bipy)]^{2+}$, which were not observed in the presence of zinc ions, or 1,10-phenanthroline (phen), or 2,2'-bipyridyl (bipy) alone. The methyl resonance of *(1)*, measured relative to the tetramethylammonium ion as reference[5], shifts by up to 0.4 or 0.25 ppm, respectively, in the presence of high concentrations of $[Zn(phen)]^{2+}$ ($\approx$0.3 M) or of $[Zn(bipy)]^{2+}$ ($\approx$0.6 M) (see Fig. 1), but much larger concentrations of Zn^{2+} (2 M) have no measurable effect. Saturated solutions of phenanthroline ($\approx$0.02 M) and of bipyridyl ($\approx$0.05 M) have a much smaller effect (*ca.* 0.02 ppm) which is however less than a third of that observed for the same concentration of $[Zn(phen)]^{2+}$ or $[Zn(bipy)]^{2+}$. Conversely, a small shift (*ca.* 0.05 ppm) in the proton resonances of $[Zn(phen)]^{2+}$ occurs; the proton NMR of phenanthroline itself is also considerably affected by the solvent environment. 3-(Trimethylsilyl)propionate *(2)* behaves in exactly the same way although the maximum shift observed is somewhat smaller, $\approx$0.3 ppm and $\approx$0.2 ppm for $[Zn(phen)]^{2+}$ and $[Zn(bipy)]^{2+}$, respectively. In the presence of $[Cu(phen)]^{2+}$ or $[Cu(bipy)]^{2+}$ the methyl resonance of *(1)* is broadened considerably and shifted, whereas the same concentration of Cu^{2+} itself has a much smaller effect.

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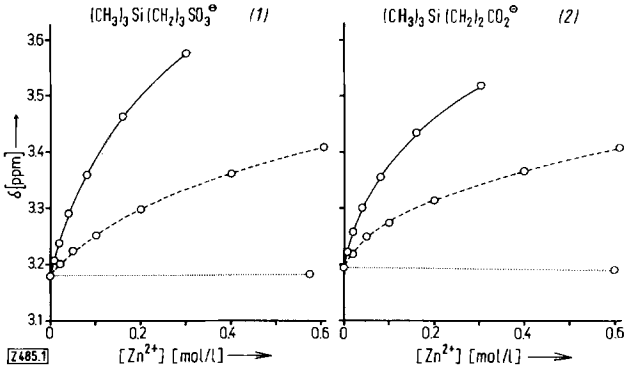

Fig. 1. Displacement of the methyl resonance in the ^{1}H-NMR spectrum of trimethylsilyl derivatives *(1)* and *(2)* (each 10^{-2} M) in the presence of Zn^{2+} (····), $[Zn(bipy)]^{2+}$ (----), or $[Zn(phen)]^{2+}$ (——) at 35 °C ($I \geq 0.1$; $NaNO_3$).

The effect on the NMR spectrum can be completely explained by the formation of ternary complexes[6] between *(1)* or *(2)* and $[Zn(phen)]^{2+}$ or $[Zn(bipy)]^{2+}$. Indeed, plotting the reciprocal of the displacement of the methyl resonance of *(2)* (data of Fig. 1) against $1/[Zn(phen)^{2+}]$ or $1/[Zn(bipy)^{2+}]$ gives $K \approx 10$ l/mol: this stability constant is about the same as is generally observed for Zn^{2+} complexes of carboxylates[7]. The results for *(1)* are consistent with a slightly lower stability appropriate for sulfonate complexes. The mutual effect of the aromatic ligand on the methyl resonance in *(1)* or *(2)* and *vice versa* indicates a hydrophobic interaction between these two moieties in the ternary complex. Comparison of the effects of Cu^{2+}, $[Cu(bipy)]^{2+}$, and $[Cu(phen)]^{2+}$ leads to the same conclusion.

Although hydrophobic interactions may have a stability as high as aromatic stacking interactions[8], they have not previously been observed in ternary complexes of metal ions: aromatic stacking interactions[6, 9] are known to affect the stability of ternary complexes[9]. In addition, ionic interactions have recently been observed in ternary complexes[10].

As even with low concentrations of trimethylsilyl reference compounds (5—10 mM), and the concentrations of metal complexes which are usually used in NMR studies (50—100 mM), shifts of up to 0.2 ppm were observed, these trimethylsilyl references should only be used circumspectly in the presence of complexes of labile metal ions.

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CAS Registry numbers:
(1), 59906-89-7; *(2)*, 59906-90-0; $[Zn(phen)]^{2+}$, 16561-55-0; $[Zn(bipy)]^{2+}$, 41849-12-1; Zn^{2+}, 23713-49-7

[1] *E. S. Hand* and *T. Cohen*, J. Am. Chem. Soc. *87*, 133 (1965).
[2] Hydrophobic interactions with the *tert*-butyl group of *tert*-butanol may also occur: the methyl resonance of *tert*-butanol is also influenced by aromatic solutes, although to a smaller extent; *R. A. Y. Jones, A. R. Katritzky, J. N. Murrell*, and *N. Sheppard*, J. Chem. Soc. *1962*, 2576.
[3] *B. R. Donaldson* and *J. C. P. Schwarz*, J. Chem. Soc. *B1968*, 395.
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[5] Similar results are obtained when acetonitrile or dioxane are used as reference; however the use of them is not so satisfactory as weak complex formation may occur with high concentrations of zinc.—The spectra were measured on a Varian Anaspect EM-360 Spectrometer at 60 MHz.
[6] *H. Sigel*, Angew. Chem. *87*, 391 (1975); Angew. Chem. Int. Ed. Engl. *14*, 394 (1975).
[7] *L. G. Sillén* and *A. E. Martell:* Stability Constants of Metal Ion Complexes. Spec. Publ. No. 17, The Chemical Society, London 1964; Suppl. No. 1, Spec. Publ. No. 25, London 1971.
[8] *E. Frieden*, J. Chem. Educ. *52*, 754 (1975).
[9] *H. Sigel* and *C. F. Naumann*, J. Am. Chem. Soc. *98*, 730 (1976).
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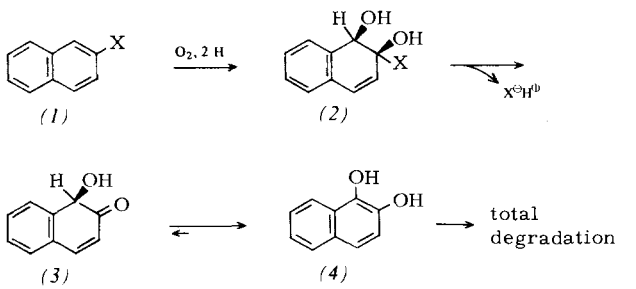
Microbiological Synthesis of (+)-*cis*-1,2-Dihydroxy-1,2-dihydronaphthalene-2-carboxylic Acid

By *Hans-Joachim Knackmuss*, *Wilhelm Beckmann*, and *Walter Otting*[*]

We recently reported the partial degradation of methylarenes by a haloarene-utilizing *Pseudomonas* strain[1]. Methyl-substituted metabolites accumulated in preparative amounts at the catabolic step corresponding to elimination of halide since the analogous elimination of the methyl anion is impossible. We can now demonstrate by another example the general applicability of this approach to the preparation of compounds which are not easily accessible by chemical synthesis.

Pseudomonas testosteroni strain A 3 (DSM 676) was isolated from sewage samples by continuous enrichment on naphthalene *(1a)* and subsequently on naphthalene-2-sulfonic acid *(1c)*. The bacterium utilizes *(1a)*, *(1c)*, or 2-naphthol *(1b)* as sole source of carbon. Induction experiments and inhibition kinetics show the organism to possess an exceptionally nonspecific naphthalene dioxygenase which hydroxylates the above substrates and channels them into the catabolic pathway of naphthalene.



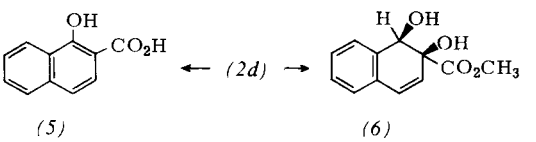
(a), X = H; *(b)*, X = OH; *(c)*, X = SO_3H; *(d)*, X = CO_2H

During the degradation of naphthalene the intermediate *(2a)* undergoes enzymatic dehydrogenation to 1,2-naphthalenediol[2]. Analogous oxygenation of *(1b)* and *(1c)* leads to labile intermediates *(2b)* and *(2c)*, respectively, which spontaneously eliminate hydroxide and hydrogen sulfite yielding *(4)* without dehydrogenation.

As a structural analog of the sulfonic acid *(1c)*, naphthalene-2-carboxylic acid *(1d)* is likewise readily hydroxylated. However, formate cannot be spontaneously eliminated from the reaction product *(2d)*, which consequently accumulates. Since the double hydroxylation requires two reduction equivalents (NAD(P)H)[2], the amount of carboxylic acid *(1d)* which can be cooxidized by resting cells is limited. Constitutively utilizable substrates providing NAD(P)H, such as succinate or malate, raise the yield of the cooxidation product.

Salicylic acid is highly suitable as a metabolizable substrate for the conversion of naphthalene-2-carboxylic acid *(1d)* on a preparative scale. Without inhibiting the turnover of *(1d)* this permits rapid bacterial growth as well as formation of reduction equivalents, and also acts as inducer of all enzymes of the naphthalene pathway, including naphthalene dioxygenase[3].

Cells of *P. testosteroni* A 3 which grow on salicylate cooxidize 2 g *(1d)*/liter without loss of activity (6.5 μmol/g protein·min). *(2d)* is formed in quantitative yield (high-pressure liquid chromatography). Acid extraction of the culture fluid with ethyl acetate gives almost pure (+)-*cis*-1,2-dihydroxy-1,2-dihydronaphthalene-2-carboxylic acid *(2d)*. Crystallization from ethyl methyl ketone furnishes colorless crystals of m.p. 147 °C [yield 74 %, $[\alpha]_D^{25} = 29.1 \pm 2°$ ($c = 1$, methanol), MS (high resolution): $M^+ = 206.0589$, calc. 206.0579][4].



Under acidic conditions, compound *(2d)* rearomatizes with elimination of water to give 1-hydroxynaphthalene-2-carboxylic acid *(5)* (>95 %). Treatment with diazomethane in ethanol/ether leads to the methyl ester *(6)* [m.p. 124 °C (from cyclohexane); MS (high resolution): $M^+ = 220.0740$, calc. 220.0736][4], which is more stable than the acid *(2d)*.

On treatment with 2,2-dimethoxypropane/HCl the methyl ester *(6)* readily affords the 1,2-isopropylidene derivative [yield 89 %, m.p. 94 °C (from hexane), $[\alpha]_D^{25} = 244° \pm 2°$ ($c = 1$, methanol), MS (high resolution): $M^+ = 260.1051$, calc. 260.1049][4].

cis-1,2-Dihydro diols have always been identified as the initial products in the metabolism of naphthalene[2] and other arenes[5] by bacteria. Only the *cis* isomer of *(2a)* reacts with 2,2-dimethoxypropane[2]. Since *(2d)* can be derivatized in corresponding manner and cell-free extracts of *P. testosteroni* only react with (+)-*cis*-*(2a)* the *cis* configuration can be deduced for *(2d)*.

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CAS Registry numbers:
(1a), 91-20-3; *(1b)*, 135-19-3; *(1c)*, 120-18-3; *(1d)*, 93-09-4; *(2a)*, 51268-88-3; *(2b)*, 59953-71-8; *(2c)*, 59953-72-9; *(2d)*, 59953-73-0; *(4)*, 574-00-5; *(5)*, 86-48-6; *(6)*, 59953-74-1; 1,2-isopropylidene derivative of *(6)*, 59953-75-2; 2,2-dimethoxypropane/HCl, 59953-76-3

[1] *H.-J. Knackmuss, M. Hellwig, H. Lackner*, and *W. Otting*, Eur. J. Appl. Microbiol. *2*, 267 (1976).
[2] *A. M. Jeffrey, H. J. C. Yeh, D. M. Jerina, T. R. Patel, J. F. Davey*, and *D. T. Gibson*, Biochemistry *14*, 575 (1975).
[3] *E. A. Barnsley*, J. Gen. Microbiol. *88*, 193 (1975).
[4] UV, IR, CD, and ^{1}H-NMR spectra are in accord with the structures given.
[5] *D. T. Gibson*, Crit. Rev. Microbiol. *1971*, 199.

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Asymmetric Synthesis of α-Substituted Ketones by Metalation and Alkylation of Chiral Hydrazones[**]

By *Dieter Enders* and *Herbert Eichenauer*[*]

Effective asymmetric synthesis with C—C coupling and simultaneous generation of a new chirality center are rare. A versatile method for the regio- and enantioselective α-alkylation of ketones is still lacking. Asymmetric alkylations *via* metal derivatives of chiral imines[1] afford only unsatisfactory chemical and optical yields of desired products.

We have now developed a method permitting the asymmetric synthesis of α-substituted ketones *(5)* in good chemical yields and in part high enantiomeric purity. The method involves conversion of the ketones *(1)* into the chiral hydra-

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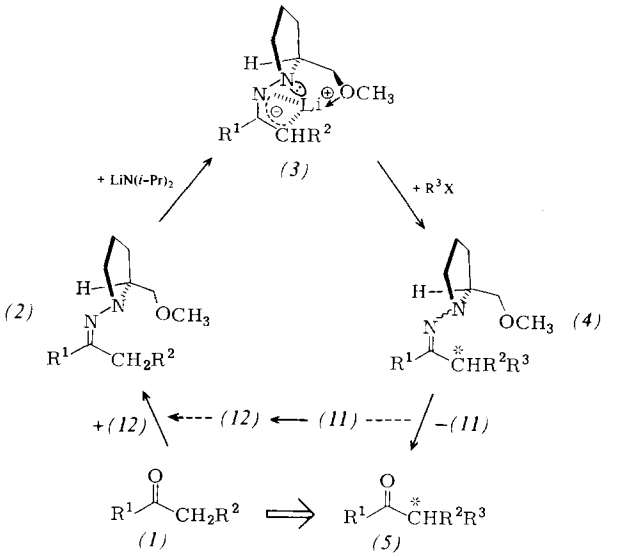
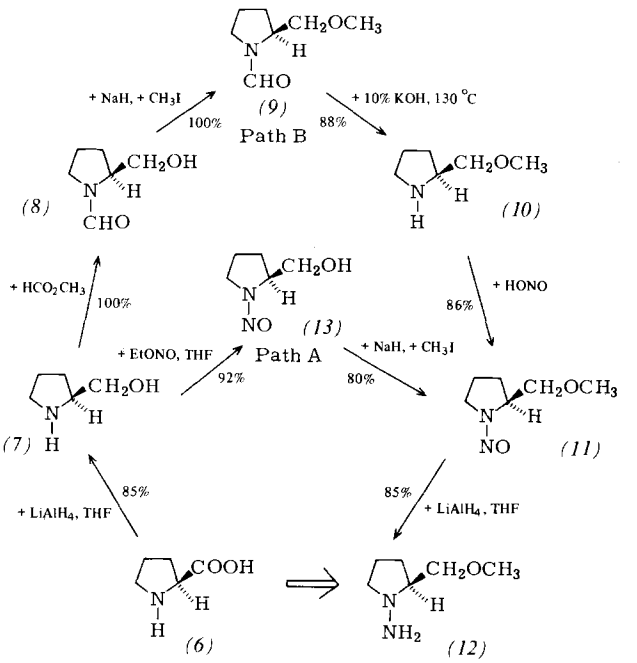
zones *(2)*, metalation with lithium diisopropylamide to the metal derivatives *(3)*[2], alkylation to *(4)*, and regeneration of the now substituted ketones *(5)* by ozonolysis or hydrolysis.

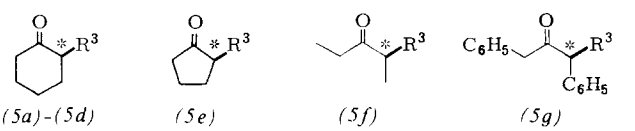




(*S*)-1-Amino-2-methoxymethylpyrrolidine *(12)*, which can be prepared in large amounts from the commercially available amino acid (*S*)-proline *(6)*, is used as chiral reagent. The total yield of *(12)* is 53% for route A, 55% for route B. In both cases purification of the (*S*)-prolinol *(7)* and the end product *(12)* by distillation suffices[3]. The chiral hydrazine *(12)* [colorless oil, b.p. 56—57°C/3 torr, ^{1}H-NMR (CCl_4): $\delta = 3.32$ (s, OCH_3), IR (film): 3340 cm^{-1} (NH_2), $[\alpha]_D^{20} = -50°$ ($c = 1$, benzene)] can be stored over a period of months in the refrigerator.

The hydrazones *(2)* and *(4)* are distillable oils[4], while the lithium compounds form colorless precipitates. Two methods are available for the step *(4)* → *(5)*. Ozonolysis at −78°C gives rise to a mixture of *(5)* and *(11)*, which after separation of the ketones *(5)* can be isolated in 80—90% yield and permits recovery of the chiral reagent *(12)*. In the alternative method reaction with excess methyl iodide generates salts of *(4)* which are hydrolyzed to *(5)* in a two-phase system (*n*-pentane/1 N HCl). The results are listed in Table 1.

The enantiomeric purity varies greatly, depending on the structure of the ketones *(1)* and R^3X. The ketones *(5a)*—*(5f)*, which are remarkably stable towards racemization, are configurationally related, since the chelates *(3)* are preferably alkylated from the "underside" of the molecule.



(5a)-(5d) *(5e)* *(5f)* *(5g)*

Table 1. Optically active ketones *(5)* prepared by asymmetric synthesis. The newly coupled C—C bonds are shown in bold print. Compounds *(4)* were generally converted into *(5)* by ozonolysis; *(5d)* and *(5f)*, however, were obtained by hydrolysis of the salts of *(4)*.

	R^3X	$[\alpha]_D^T$ (*c*, solvent) [a]	Yield [%] [b] optical	chemical
(5a)	$(CH_3)_2SO_4$	− 11.9^{23} (2.5, MeOH) + 14 (0.23, MeOH) [5]	85 (*R*)	80 (70)
(5a)	CH_3I	− 9.7^{20} (neat) − 15.22^{20} (neat) [1a]	64 (*R*)	82 (73)
(5b)	C_2H_5I	− 30^{20} (0.5, MeOH) [c]	>50 (*R*)	80 (71)
(5c)	*n*-C_3H_7I	− 24.3^{20} (4.2, MeOH) − 27.9^{20} (MeOH) [6]	87 (*R*)	81 (73)
(5d)	$CH_2{=}CHCH_2Br$	− 11.2^{22} (2.05, MeOH) − 13.7$^{27.5}$ (2.04, MeOH) [1b, 6]	82 (*S*)	67 (60)
(5e)	CH_3I	− 50^{23} (1.0, MeOH) −110.5^{25} (1.19, MeOH) [7]	45 (*R*)	82 (74)
(5f)	C_2H_5I	+ 19.2^{20} (2.5, ether) + 32.1^{20} (2.5, ether) [8]	60 (*S*)	76 (66)
(5g)	CH_3I	+ 88^{20} (1.0, benzene)	30 [d]	81 (70)

[a] First value: rotation of the distilled, spectroscopically and gas-chromatographically pure ketones. Second value: rotation quoted in the literature (values in degrees).

[b] Chemical yields based on chiral hydrazone *(2)*. In brackets: total yields.

[c] Values by *R. Kuhn, H. E. Driesen,* and *H. J. Haas,* Justus Liebigs Ann. Chem. *718*, 98 (1968): ORD ($c = 0.5$, MeOH), $[\alpha]^{20}$ (nm) = +992° (268), −878° (307). Under the same conditions we found the values: +492° (268), −430 (307) = 50% enantiomeric purity; since this value deviates greatly from those of the other 2-alkylcyclohexanones we believe that our product has a greater optical purity than 50%.

[d] Determined NMR spectroscopically with the shift reagent tris[3-(heptafluoro-1-hydroxybutylidene)-(d)-camphorato]europium(III) (Aldrich).

(R)-2-n-Propylcyclohexanone (5c) from cyclohexanone

Compound *(12)* (2.6 g, 20 mmol) is treated with cyclohexanone (2.19 ml, 21 mmol) with stirring at room temperature and then heated to 60 °C for 8 h. The crude product is dissolved in CH_2Cl_2 and the resulting solution dried over sodium sulfate, concentrated in a rotary evaporator, and finally distilled. *(2)*, $R^1/R^2 = -(CH_2)_4-$, is obtained in 90 % yield (3.78 g) as a colorless oil, b. p. 72—73 °C/0.025 torr, $[\alpha]_D^{20} = +290°$ ($c = 0.5$, benzene). *(2)* (2.1 g, 10 mmol) is added dropwise with stirring at 0 °C to a solution of lithium diisopropylamide (prepared from 6.5 ml 1.6 N *n*-butyllithium solution and 1.7 ml diisopropylamine in 50 ml tetrahydrofuran at 0 °C). After 2 h the reaction mixture is cooled to −100 °C and 1.0 ml (10.5 mmol) of *n*-propyl iodide is added dropwise. The mixture is stirred for a further 3 h, allowed to warm to room temperature, treated with ether, dried over magnesium sulfate and the solvent removed. A solution of the crude product in CH_2Cl_2 (50 ml) is cooled to −78 °C and treated with ozone until the solution is colored blue. After removal of excess ozone by introduction of argon, warming, and concentration, *(5c)* is separated from the nitrosamine *(11)* by molecular distillation over glass wool (oil bath temperature 125 °C/18 torr).

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CAS Registry numbers:
(1a), 108-94-1; *(1e)*, 120-92-3; *(1f)*, 96-22-0; *(1g)*, 102-04-5; *(2a)*, 59983-34-5; *(2e)*, 59983-35-6; *(2f)*, 59983-36-7; *(2g)*, 59983-37-8; *(5a)*, 22554-29-6; *(5b)*, 22617-19-2; *(5c)*, 36302-45-1; *(5d)*, 36302-35-9; *(5e)*, 39947-50-7; *(5f)*, 20086-34-4; *(5g)*, 59983-38-9; $(CH_3)_2SO_4$, 77-78-1; CH_3I, 74-88-4; C_2H_5I, 75-03-6; *n*-C_3H_7I, 107-08-4; $CH_2{=}CHCH_2Br$, 106-95-6; *(12)*, 59983-39-0

[1] a) *D. Méa-Jacheet* and *A. Horeau*, Bull. Soc. Chim. Fr. *1968*, 4571; b) *M. Kitamoto, K. Hiroi, S. Terashima*, and *S. Yamada*, Chem. Pharm. Bull. *22*, 459 (1974).
[2] See *E. J. Corey* and *D. Enders*, Tetrahedron Lett. *1976*, 3, 11; *E. J. Corey, D. Enders*, and *M. G. Bock*, *ibid. 1976*, 7.
[3] Preparation of *(11)* *via* route A: *H. Hartmann*, Examensarbeit, Universität Giessen 1974; *(11)* has also been reported by *T. Połoński* and *K. Prajer* (Tetrahedron *32*, 847 (1976)).
[4] The new compounds *(2)* and *(4)* and *(8)*–*(13)* give correct elemental analyses; IR, NMR, and mass spectra are in agreement with the given structures.
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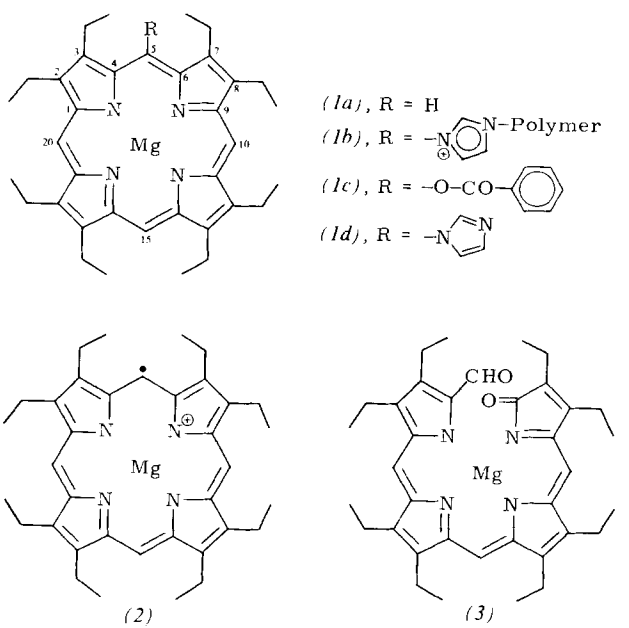
[7] *J. J. Partridge, N. K. Chadha*, and *M. R. Uskoković*, J. Am. Chem. Soc. *95*, 532 (1973).
[8] *F. Nerdel* and *E. Henkel*, Chem. Ber. *86*, 1002 (1953); *M. Teschner*, Diplomarbeit, Universität Giessen 1972.
[9] *Note added in proof: A. I. Meyers et al.* have reported the enantioselective alkylation of cyclohexanone *via* lithiated enamines, J. Am. Chem. Soc. *98*, 3032 (1976).

Reaction of Magnesium Porphyrinates in Polymers Containing Imidazole

By *S. Besecke, B. Evans, G. H. Barnett, K. M. Smith*, and *J.-H. Fuhrhop*[*]

The π radicals of magnesium porphyrinates, *e. g.* of protochlorophyll and chlorophyll a, play a central role in the biosynthesis of chlorophylls[1] and in photosynthesis[2]. In biological systems the chromophores are bound to proteins or lipoproteins which embed the highly reactive radicals in a hydrophobic matrix and thus protect them from irreversible destruction by external nucleophiles such as water. We have studied the reactions of magnesium octaethylporphyrin *(1a)* (as the simplest chlorophyll model) in synthetic copolymers of styrene and 1-vinylimidazole (as a model for hydrophobic, possibly electron-conducting[3] protein components), the proportion of imidazole being varied between 0.1 and 20 mol %.

Irradiation of *(1a)* in a solid matrix of polystyrene containing 0.1 % or less of 1-vinylimidazole in the presence of oxygen rapidly gives rise to the previously characterized compound formylbiliverdin *(3)*[4] in more than 80 % yield, *i. e.* the magnesium porphyrin added molecular oxygen at its periphery. Use of a copolymer containing 20 % of imidazole under otherwise identical conditions led to quantitative conversion of *(1a)* into its π radical cation *(2)*[2] within one hour. No addition of oxygen took place. Dissolution of the polymer-porphyrin mixture in benzene and reduction with triethylamine regenerated the magnesium porphyrin *(1a)* in over 80 % yield. Both the radical *(2)* and formylbiliverdin *(3)* were stable for months in the solid polymer, while they quantitatively decomposed within a few hours in solution.



(2)

(3)

Chemical oxidation of *(1a)* with benzoyl peroxide in a benzene solution containing the polymer with 20 % imidazole took a different course. Although the radical cation *(2)* was again generated initially, it immediately reacted with the polymer to form new covalent bonds. Shaking of the resulting solution with 10 % hydrochloric acid containing 50 % of ethanol did demetalate the polymer-bound magnesium porphyrin, but the porphyrin dication could not be transferred to the water/ethanol phase. Our explanation of this behavior assumes that benzoyl peroxide oxidizes not only the magnesium porphyrin *(1a)* to the radical *(2)* but also the imidazole to the imidazole radical. The two radicals then react together to form *(1b)*.

In order to confirm the formation of *(1b)* we oxidized a mixture of *(1a)* and imidazole in chloroform with benzoyl peroxide. Apart from 20% of 5-benzoyloxyporphyrin *(1c)* we obtained 60 % of the expected 5-imidazolyl derivative *(1d)*.

On the basis of these findings we suspect that in biological systems chlorophyll is protected from irreversible autoxidation not only by carotenes but also by surrounding proteins, and that addition of imidazole and protein constituents of similar

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reactivity could play a role in the hitherto little investigated biological degradation of chlorophylls.

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(1a), 20910-35-4, *(1c)*, 60064-52-0; *(1d)*, 60064-53-1; *(1e)*, 60031-40-5; *(1f)*, 60031-41-6; *(2)*, 34606-97-8; *(3)*, 54000-75-8

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[2] *J.-H. Fuhrhop*, Angew. Chem. *86*, 363 (1974); Angew. Chem. Int. Ed. Engl. *13*, 321 (1974).
[3] *M. E. Winfield*, J. Mol. Biol. *12*, 600 (1965).
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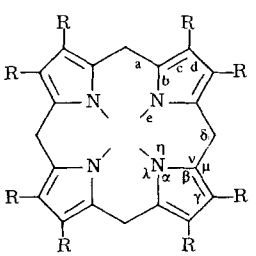
Structure of *N,N,N',N'''*-Tetramethyl-2,3,7,8,12,13,17,18-octakis(carboxymethyl)porphyrinogen Dihydrate[**]

By *Gisela Sawitzki* and *Hans Georg von Schnering*[*]

Franck and *Wegner* recently succeeded in preparing cyclic tetrapyrroles with four *N*-methyl groups for the first time[1]. We have carried out an X-ray structure analysis on a representative of this long-sought class of compounds[2], *viz.* *N,N',N'',N'''*-tetramethyl-2,3,7,8,12,13,17,18-octakis(carboxymethyl)porphyrinogen *(1)*, which crystallizes as the dihydrate.



(1),
R = CH_2–COOH

(1) crystallizes in the monoclinic space group I2/c-C_{2h}^6 with $a=15.914(3)$, $b=18.288(4)$, $c=14.387(3)$ Å, $\beta=109.61(2)°$, and $Z=4$ molecules per unit cell. The structure was solved by direct methods (MULTAN)[3] and refined[5] to $R=0.065$ for 1755 reflections with $I>2\sigma(I)$ (four-circle diffractometer SYNTEX-$P\bar{1}$, CuKα, ω-scan, $2\theta_{max}=100°$[4]). After anisotropic refinement of the heavy atoms N, C, and O, the greater part of the H atoms could be located in a ΔF map. The H atoms were included in the last cycles of refinement with average isotropic thermal parameters.

The molecule displays crystallographic C_2-symmetry. The mean distances and angles in the skeleton are [cf. formula *(1)*] $a=1.506(7)$, $b=1.385(8)$, $c=1.373(6)$, $d=1.416(2)$, $e=1.462(9)$ Å; $\alpha=109.1(1)$, $\beta=107.6(5)$, $\gamma=107.9(3)$, $\delta=116.2(8)$, $\lambda=126.6(1)$, $\eta=124.1(3)$, $\nu=123.0(17)$, and $\mu=129.0(11)°$. The normals of the pyrrole rings are inclined by 61 and by 65°, respectively, to the C_2 axis of the molecule. Two of the *N*-methyl groups are rigidly fixed by neighboring groups, the other two show free rotation within a range of ±30° (the H atoms of these groups appeared as diffuse maxima). The shortest H—H distances between different groups are about 2.2 Å.

The porphyrinogen skeleton is "bridged" by two symmetrically equivalent side chains and two molecules of water (cf. Fig. 1), the carboxyl groups of the side chains being linked

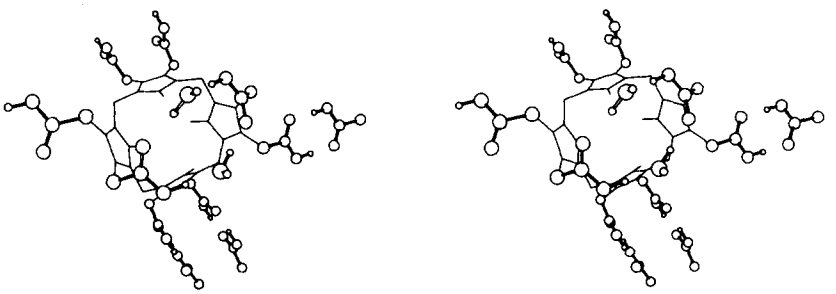


Fig. 1. Stereoscopic representation (ORTEP [6]) of a molecule, viewed almost along the C_2 axis. The porphyrinogen skeleton is outlined. The atoms of the side chains and the H_2O molecules are represented by circles. In the upper part the mutual orientation of COOH groups and H_2O molecules (H bonds omitted) can be recognized. The intermolecular H bonds are indicated for selected COOH groups of neighboring molecules.

to the H_2O molecules by hydrogen bonds (O—O distances = 2.6 and 2.8 Å). The H_2O molecules and the COOH groups are both proton donors and proton acceptors. The other carboxyl groups of the side chains are likewise connected by hydrogen bonds with carboxyl groups of four neighboring molecules (O—O distances = 2.6 to 2.7 Å). In this way an infinite two dimensional molecular lattice is built up. This result accords with the ready cleavage of the crystals along their needle axis.

In our opinion the intramolecular hydrogen bonds between COOH groups and H_2O molecules contribute substantially to the stabilization of the unusual conformation.

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CAS Registry numbers:
(1), 60004-32-2

[1] *B. Franck* and *Ch. Wegner*, Angew. Chem. *87*, 419 (1975); Angew. Chem. Int. Ed. Engl. *14*, 424 (1975).
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[3] *G. Germain, P. Main,* and *M. M. Woolfson*, Acta Crystallogr. *A 27*, 368 (1971).
[4] We are grateful to Dr. *K. Peters* (Stuttgart) for measuring the intensities.
[5] IBM 360/50 computer (Universität Münster) and NOVA 1200 computer with the XTL program system (SYNTEX); Anorganisch-chemisches Institut der Universität Münster.
[6] *C. K. Johnson*, ORTEP-ORNL 3794, Oak Ridge National Laboratory, Oak Ridge, Tennessee, ORTEP II version (1971).

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Indirect Determination of the Half-Wave Reduction Potentials of Benzene and [2.2]Paracyclophane[**]

By *Fabian Gerson, Hiroaki Ohya-Nishiguchi,* and *Christoph Wydler*[*]

The half-wave reduction potential $E_{1/2}$ of benzene lies in a range (< −3 V) which is inaccessible for polarographic stu-

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dies. A "theoretical" estimate of this value can be obtained by extrapolation from the linear relationship (1) between the observed half-wave reduction potentials $E_{1/2}$ of conjugated π-systems and the calculated energies of the lowest unoccupied orbitals (LUMOs).

$$E_{1/2} = -0.92 + 2.37x \text{ [volt]} \quad (1)$$

The values $E_{1/2}$ are polarographic data measured against the saturated calomel electrode, and the numbers x characterize the HMO energies ($\alpha + x\beta$) of the LUMOs[1]. The half-wave reduction potential of benzene ($x = -1.00$) resulting by extrapolation from eq. (1) is -3.29 V.

The finding[2] that benzene can also be electrolytically reduced in an ethereal solvent to its radical anion suggests an analogous, "experimental" procedure for the evaluation of the half-wave potential. A prerequisite for such a procedure is a linear relationship between the minimum voltages V_a, at which the ESR spectra of the radical anions appear during the electrolysis, and the polarographic data $E_{1/2}$. That this prerequisite has been met is shown by the appearance voltages V_a measured in the present work for the radical anions of 20 hydrocarbons and plotted in Figure 1 *vs.* the corresponding values $E_{1/2}$. The pertinent regression line has the equation

$$V_a = (1.92 \pm 0.06) E_{1/2} \quad (2)$$

with a correlation coefficient of 0.991 and a deviation from the origin (0.007) which is far below the significance threshold.

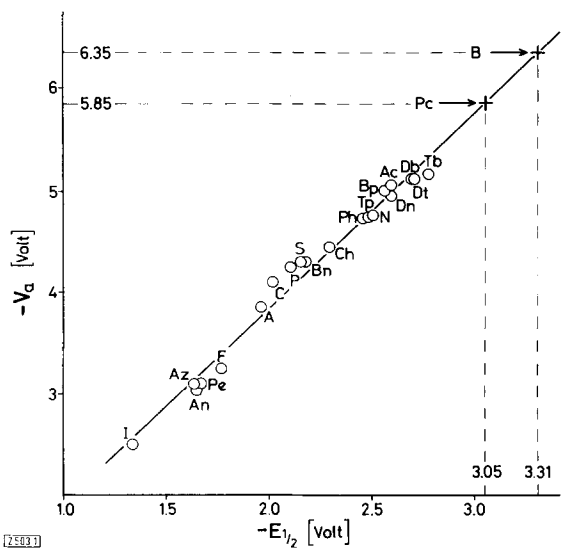

Fig. 1. Plot of appearance voltages V_a *vs.* half-wave reduction potentials $E_{1/2}$. A = anthracene; Ac = acenaphthene; An = acenaphthylene; Az = azulene; B = benzene; Bn = biphenylene; Bp = biphenyl; C = coronene; Ch = chrysene; Db = 4,4'-dimethylbiphenyl; Dn = 2,3-dimethylnaphthalene; Dt = 4,4'-di-*tert*-butylbiphenyl; F = fluoranthene; I = indeno[1,2,3-*cd*]fluoranthene; N = naphthalene; P = pyrene; Pc = [2.2]paracyclophane; Pe = perylene; Ph = phenanthrene; S = stilbene; Tb = 3,3',5,5'-tetra-*tert*-butylbiphenyl; Tp = triphenylene.

The half-wave reduction potentials $E_{1/2}$ in equation (2) and Figure 1 were either taken from the compilation by *Streitwieser*[1] or determined in a laboratory of our Department[3, 4]. They refer to the saturated calomel electrode as standard. On the other hand, the appearance voltages V_a are not bound to any conventional reference level and may thus be compared only with data obtained under the same conditions. The electrolytic cell used throughout the entire series had a cylindrical form and contained a helical cathode of amalgamated gold, along with an anode of platinum wire placed along the cell axis[5]. 1,2-Dimethoxyethane and 0.1 M tetrabutylammonium perchlorate served as the solvent and supporting salt, respectively. The temperature was -90 °C. According to the original quantity weighed in, the concentration of each hydrocarbon ought to be 5×10^{-3} mol/liter. However, in the case of some aromatics of poor solubility, the actual concentration was lower, which may be one of the reasons for the deviation of the corresponding data V_a from the regression line in Figure 1. For each hydrocarbon several measurements were performed in order to determine the minimum value for the appearance voltage V_a. Such a value was considered as reliable when it could be reproduced within an experimental error of ± 0.05 V.

Extrapolation of the equation (2) to the appearance voltage V_a (Fig. 1) for the radical anion of benzene yields $E_{1/2} = -3.31 \pm 0.12$ V (90% confidence limits) as an "expermental" estimate of the half-wave reduction potential of benzene in excellent agreement with the "theoretical" result of -3.29 V. Obviously, values of $E_{1/2}$ can be estimated in a similar way for other compounds of low electron affinity, provided that such compounds are electrolytically convertible into their radical anions. An example is [2.2]paracyclophane for which equation (2) affords a half-wave reduction potential $E_{1/2} = -3.05 \pm 0.12$ V (Fig. 1). It is worth mentioning that in this case an extrapolation of equation (1) is not as straightforward as for benzene, since the HMO model is not directly applicable to [2.2]paracyclophane. The values $E_{1/2}$ found for the two hydrocarbons are in accord with a previous report which points to a distinctly higher electron affinity of [2.2]paracyclophane relative to that of benzene[6].

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CAS Registry numbers:
Benzene, 71-43-2; [2.2]paracyclophane, 1633-22-3

[1] *A. Streitwieser, Jr.*: Molecular Orbital Theory for Organic Chemists. Wiley, New York 1961, Chapter 7.1.
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[4] The polarographic measurements were performed by Drs. *H. G. Seiler* and *H. R. Schmutz* of the Anorganisch-Chemisches Institut, Basel. For biphenyl the value $E_{1/2}$ (-2.57 V) determined by these workers was used instead of that (-2.70 V) listed in ref. [1].
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Isolation and Infrared Spectrum of Iodine Azide

By *Kurt Dehnicke*[*]

Far less is known about the chemistry of iodine azide than about that of chlorine azide and bromine azide[1]. The preparation of IN_3 from iodine and silver azide in ether, which leads to very readily decomposable solutions, has been reported[2], as has the ability of IN_3 to undergo stereospecific addition to olefinic double bonds, for which IN_3 generated from sodium azide and iodine chloride in acetonitrile is employed *in situ*[3].

We have found that solutions of iodine azide in dichloromethane, carbon tetrachloride, and benzene are much more stable than those in ether. 1 to 3% solutions are obtained by dropwise addition with stirring at 0 °C of I_2 solutions of corresponding concentration to freshly precipitated silver azide freed from water. Solutions of this concentration can be manipulated without danger, and can even be dried without decomposition over phosphorus pentoxide.

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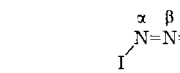
Careful evaporation of solvent CH_2Cl_2 leaves a residue of golden yellow, hygroscopic, and somewhat light-sensitive needle-shaped and extensively intermeshed crystals of IN_3, of which only very small amounts were prepared owing to their explosive nature. Under normal pressure they can be sublimed at room temperature on to a cold finger maintained at −78 °C. No melting point can be recorded because the sublimation point lies at 24 °C/760 torr.

The IR spectrum of IN_3 recorded both in solution and in Nujol emulsion (Table 1) is compatible with the structure *(1)* which is bent at the α-N atom and has the molecular symmetry C_s.



(1)

Table 1. IR spectrum of iodine azide (C_s symmetry).

In benzene [cm^{-1}]	Intensity	Crystalline [cm^{-1}]	Intensity	Assignment	
3242	w	3242	vw	$\nu_{as}+\nu_s(N_3)$	
		2460	vw	$2\times\nu_s(N_3)$	
2058	vs	2045	vs	$\nu_{as}(N_3)$	A′
1176	m	1240	m	$\nu_s(N_3)$	A′
		648	vw	$\delta(N_3)$	A′
578	w	580	w	$\gamma(N_3)$	A″
338	m	338	m	ν(N—I)	A′

Apart from the INN deformation vibration (A′) to be expected below the range of measurement (down to 250 cm^{-1}) all the fundamental vibrations can be assigned. Two special features of the spectrum warrant attention:

1) The two N_3 stretching vibrations having symmetric and asymmetric character move apart significantly during the transition solid/dissolved. This might be connected with a favoring of the diazonium structure of IN_3 in the dissolved state. However, an intermolecular interaction is more likely and would lead to deviation from linearity of the NNN group in the crystalline state, as observed for some heavy metal azides[4].

2) The I—N stretching frequency lies at 338 cm^{-1} and thus at considerably longer wavelengths than to be expected from the series FN_3 [ν(FN) = 869 cm^{-1}][5], ClN_3 [ν(ClN) = 719 cm^{-1}][5, 6], BrN_3 [ν(BrN) = 687 cm^{-1}][5]. This result can be explained by a pronounced polarity of the iodine-nitrogen bond as shown in *(2)*.

(2)

Iodine azide should therefore react with metal iodides *via* substitution. Indeed boron triiodide and iodine azide immediately deposit I_2 and form the unknown compound diiodine borazide[7].

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CAS Registry numbers:
IN_3, 14696-82-3

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[7] *K. Dehnicke* and *W. Siebert*, unpublished.

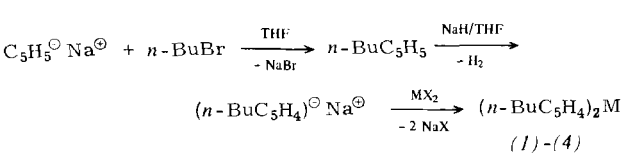
A New Probe for C-C Hyperconjugation: ^{13}C-NMR on Paramagnetic Metallocenes[1]

By *Karl Eberl*, *Frank Herwig Köhler*, and *Lothar Mayring*[*]

On the basis of *Mulliken*'s concept of hyperconjugation[2], C-C hyperconjugation can be regarded as a particularly important variant of this phenomenon. It warrants attention in the large number of organic and organometallic compounds in which C-C σ bonds can interact with π orbitals of aromatic systems or heteroatoms. The Baker-Nathan effect was considered to be an especially significant indication of hyperconjugation, C-C hyperconjugation being thought much smaller than C-H hyperconjugation[3]. However, this effect was found to arise rather from changes in solvation[4]. Very recent *ab initio* calculations even show C-C hyperconjugation to make an important contribution to the stability of acetyl cations[5]. This situation has long awaited experimental elucidation.

The development of paramagnetic ^{13}C-NMR spectroscopy[6] now permits study of C-C hyperconjugation with the aid of a generally applicable method. Suitable molecules are paramagnetic metallocenes. In these compounds part of the spin density of the unpaired electrons is delocalized into the π system of the ligand. From that position there exists the possiblity of hyperconjugational transfer to the β-C atoms of substituents located on the cyclopentadienyl groups. In this way the unpaired spin density becomes an indicator of C-C hyperconjugation. It causes exceptionally large ^{13}C shifts $\delta(^{13}C)$ which serve as a sensitive probe.

A versatile test is possible with *n*-butyl-substituted metallocenes. These compounds contain not only β-C but also γ-C and δ-C atoms, which are hardly affected by C-C hyperconjugation. The hitherto unknown 1,1′-di-*n*-butyl metallocenes of vanadium *(1)*, chromium *(2)*, cobalt *(3)*, and nickel *(4)* can be obtained in 50 to 80 % yield by the following method (yield of intermediates: 42 and 75 %)[6].



(1)–*(4)*

Compounds *(1)* to *(4)* are highly air-sensitive, deeply colored liquids. Elemental analyses confirm their purity, and ^{13}C-NMR spectra their molecular structure (typical example in Fig. 1). The precise $\delta(^{13}C)$ are listed in Table 1. Their assignment follows from the chemical shifts, intensities, and multiplicities, as well as from earlier findings[6].

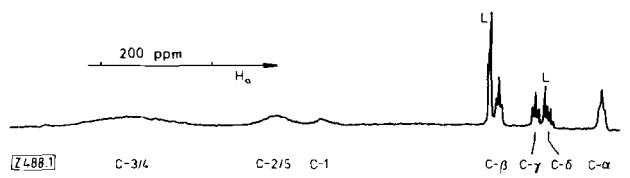


Fig. 1. ^{13}C-NMR spectrum of $(n\text{-}BuC_5H_4)_2Co$ *(3)* at 309 K. L = [D_8]-toluene. Concerning assignment, see Fig. 2.

In order to facilitate comparison of *(1)*—*(4)* we converted the $\delta(^{13}C)$ values in the known way[7, 8] into hyperfine interaction constants *A*. In connection with C-C hyperconjugation we are interested in the magnitudes of *A* at the *n*-butyl C atoms. The curves plotted in Fig. 2 reveal that |*A*| is excep-

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Table 1. Paramagnetic ^{13}C shifts [a] of *n*-butyl-metallocenes.

Cpd.	M	Position [b] C-1	C-2/5	C-3/4	C-α	C-β	C-γ	C-δ
(1)	V	+475	+725	+538	−745	−405	−25	−20
(2)	Cr	+100	+475	+348	−458	− 99	+ 5	− 3
(3)	Co	−334	−433	−706	+117	− 73	−15	+ 2
(4)	Ni	[c]	[c]	[c]	+612	−380	−40	+ 2

[a] Measured in ppm relative to solvent ([D_8]-toluene), converted to shifts relative to 1,1'-di-*n*-butylferrocene; downfield shifts negative; temperature 309 K; instrument: Bruker HX 90; digital accuracy 1 ppm/data point.
[b] Cf. Fig. 2.
[c] Not yet observed owing to excessive line width.

tionally large at β-C. The selective transfer of unpaired spin density to C-β is due to C-C hyperconjugation.

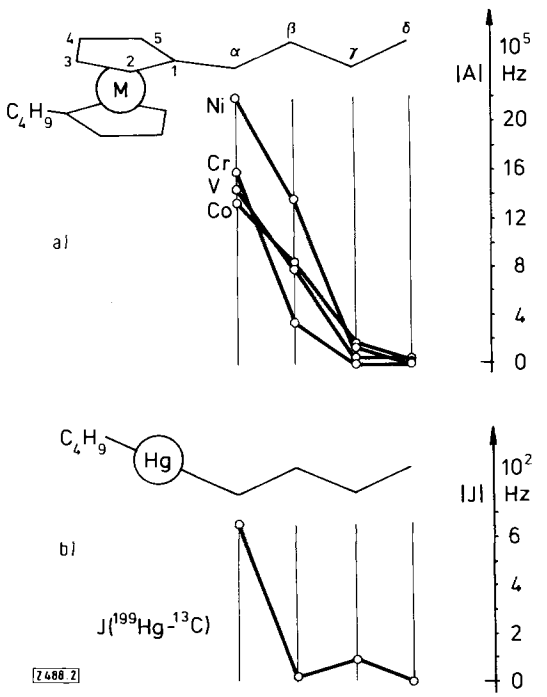

Fig. 2. a) Electron spin transfer into the *n*-butyl group of the paramagnetic metallocenes *(1)* to *(4)* with C-C hyperconjugation. b) Nuclear spin transfer into the *n*-butyl group of $(n\text{-Bu})_2Hg$ without C-C hyperconjugation.

For the sake of substantiation we also consider the comparison with the nuclear coupling constants $J(^{199}Hg\text{-}^{13}C)$ of di-*n*-butylmercury[9] (cf. Fig. 2). Both the nuclear spin coupling and the delocalization of unpaired electrons are mediated by Fermi contact interaction[10]. In contrast to the metallocenes *(1)* to *(4)* no C-C hyperconjugation to the β-C atom is to be expected in di-*n*-butylmercury[11]; $^2J(^{199}Hg\text{-}^{13}C)$ is accordingly very small in Figure 2.

^{13}C-NMR measurements on paramagnetic molecules is a versatile and rapid probe for C-C hyperconjugation; the natural abundance of ^{13}C suffices for the measurements. We are therefore attempting to derive quantitative results.

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CAS Registry numbers:
(1), 60064-84-8; *(2)*, 60064-85-9; *(3)*, 60064-86-0; *(4)*, 60064-87-1; ^{13}C, 14762-74-4

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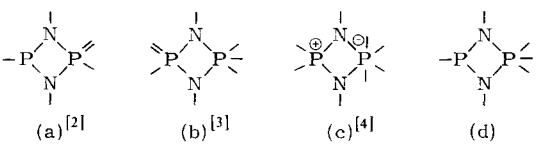
[11] $^3J(^{199}Hg\text{-}^{13}C)$ shows slight hyperconjugation to γ-C.

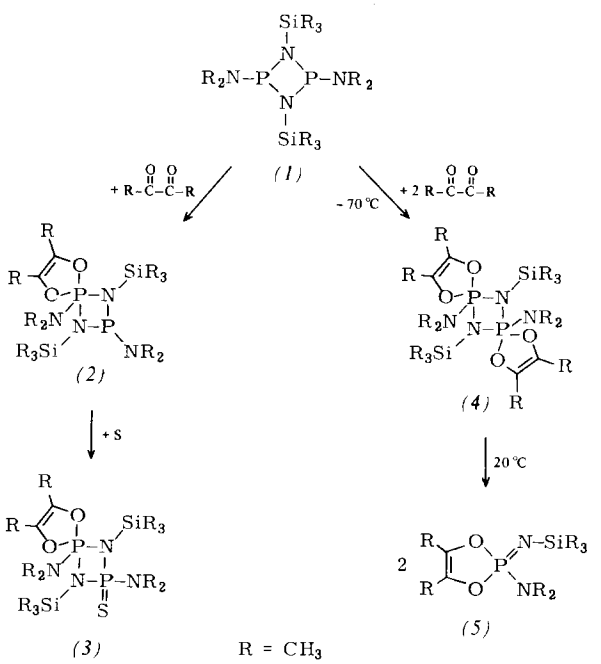
Isolation of a Diaza-λ^3,λ^5- and a Thermodynamically Unstable Diaza-λ^5,λ^5-diphosphetidine

By *Werner Zeiss*[*]

The chemistry of the diazadiphosphetidines[1] has recently been extended to include compounds of the type *(a)*—*(c)*, the two phosphorus atoms possesing different oxidation and/or coordination numbers.



Partial oxidation of the diaza-λ^3,λ^3-diphosphetidine *(1)* recently prepared by us[5] with biacetyl yields a compound of type *(d)*, namely the diaza-λ^3,λ^5-diphosphetidine *(2)*. As expected, P^{III} in *(2)* is still readily oxidizable: reaction with sulfur leads quantitatively to *(3)*, a further diazadiphosphetidine of type *(b)* (Table 1).



(1) reacts smoothly with an excess of biacetyl at low temperature to give the isolable diaza-λ^5,λ^5-diphosphetidine *(4)*, which, in solution at room temperature, decomposes quantitatively within 24 h to the monomeric phosphazene *(5)*. In contrast to crystalline *(4)*, *(5)* is a colorless liquid which crystallizes at −27 °C and does not re-dimerize to *(4)*, even in the crystalline state (Table 1).

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Table 1. Properties of the compounds *(1)*—*(5)*. NMR [a]: *(1)*—*(3)* in CH_2Cl_2, *(4)* and *(5)* in $CDCl_3$.

Cpd.	M.p. [°C]	$\delta^{31}P$ [ppm] P^{III}	P^{V}	J_{PP} [Hz]	$\delta^{1}H$ [ppm] $SiCH_3$	$NCH_3(P^{III})$	$NCH_3(P^{V})$	CH_3 (Ring)	J_{PH} [Hz] PNSiCH	$P^{III}NCH$	$P^{V}NCH$
(1)	30	−107.6			0.075 (t)	2.72 [e]			0.5	8.4 [g]	
(2)	52	− 84.3	+40.6 [b]	15	0.100 (d)	2.59 (d)	2.81 (d)	1.76 (s)	0.8	7.8	10.8
(3)	93—94		+51.8 [b]	[d]	0.216 (s)		2.80 (d) [f]	1.80 (s)	[d]		11.9
			−51.7 [c]				2.83 (d) [f]				11.7
(4)	76—78 (dec.)		+53.1 [b]		0.090 (s)		2.73 [e]	1.78 (s)	[d]		10.9 [g]
(5)	−27		−15.9 [c]		0.038 (s)		2.67 (d)	1.87 (s)	[d]		11.2

[a] Shifts w.r.t. H_3PO_4 (external) or TMS (internal) as standard; $\delta^{31}P$ to higher field, $\delta^{1}H$ to lower field quoted as positive.
[b] Coordination number 5.
[c] Coordination number 4.
[d] Not observed.
[e] $[X_6A]_2$ spin system.
[f] Arbitrary assignment.
[g] $J = J_{PNCH} + J_{PNPCH}$.

The thermodynamic instability of *(4)* compared to that of its monomer *(5)* is consistent with expectation, since the presence of bulky groups on nitrogen[6] together with electron-donor groups on phosphorus is known to inhibit dimerization of a phosphazene in all cases investigated so far. However, under the mild conditions mentioned the reaction sequence *(1)*→*(4)*→*(5)* evidently runs kinetically controlled, thus permitting isolation of *(4)*.

2,4-Bis(dimethylamino)-6,7-dimethyl-1,3-bis(trimethylsilyl)-5,8-dioxa-1,3-diaza-2λ³,4λ⁵-diphosphaspiro[3.4]oct-6-ene (2)

A solution of *(1)* (1.9 g, 5.85 mmol) in anhydrous CH_2Cl_2 (5 ml) is cooled with stirring to −70 °C. The solution is then treated with biacetyl (0.5 g, 5.82 mmol) and allowed to warm to room temperature. After removal of solvent *in vacuo* *(2)* can be crystallized from a minimal amount of acetonitrile as colorless crystals: yield 1.3 g (54 %), m.p. 52 °C (sealed tube).

5,7-Bis(dimethylamino)-2,3,9,10-tetramethyl-6,12-bis(trimethylsilyl)-1,4,8,11-tetraoxa-6,12-diaza-5λ⁵,7λ⁵-diphosphadispiro-[4.1.4.1]dodeca-2,9-diene (4)

To a stirred solution of *(1)* (4.75 g, 14.7 mmol) in anhydrous CH_2Cl_2 at −75 °C is added 2.7 g (31.4 mmol) biacetyl. Crystals begin to form almost immediately. On completion of crystallization the reaction product is allowed to warm to −30 °C, whereupon total dissolution takes place. The solution is covered with dry acetonitrile (30 ml) and allowed to stand for 24 h at −20 °C. The colorless crystals which are formed, and which can be stored almost indefinitely at −20 °C, are filtered off on a Gooch frit in the absence of moisture and dried *in vacuo* at room temperature. Yield of *(4)*: 3.2 g (44 %), m.p. 76—78 °C (dec.) (sealed tube).

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(1), 59992-09-5; *(2)*, 59992-10-8; *(3)*, 59992-11-9; *(4)*, 60004-39-9; *(5)*, 59992-12-0; $CH_3COCOCH_3$, 431-03-8

[1] Summary: *A. F. Grapov, N. N. Melnikov*, and *L. V. Razvodovskaya*, Russ. Chem. Rev. *39*, 20 (1970).
[2] *R. Keat et al.*, J. Chem. Soc. Dalton Trans. *1973*, 1414; *E. Niecke* and *O. J. Scherer*, Nachr. Chem. Tech. *23*, 395 (1975); *R. Appel* and *M. Halstenberg*, J. Organomet. Chem. *99*, C25 (1975); *E. Niecke* and *W. Bitter*, Chem. Ber. *109*, 415 (1976); *E. Niecke* and *W. Flick*, J. Organomet. Chem. *104*, C23 (1976).
[3] *R. Appel* and *M. Halstenberg*, Angew. Chem. *87*, 810 (1975); Angew. Chem. Int. Ed. Engl. *14*, 768 (1975).
[4] *R. Schmutzler et al.*, J. Chem. Soc. Dalton Trans. *1974*, 2153.
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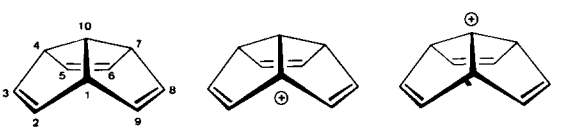
Stability of Triquinacenyl Cations and Triquinacenyl Radicals

By *Peter Bischof*[*]

In nonplanar π-systems the σ-π interactions can not be neglected. It will be shown here, for example, that this interaction is important in the bridgehead cations *(2)* (1-triquinacenyl cation) and *(3)* (10-triquinacenyl cation) and in the corresponding radicals *(2')* and *(3')*.



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

The structures of *(2)* and *(3)* were optimized by MINDO/3 calculations[1]. The structural data of the geometries obtained are listed in Table 1. The calculation reveals that the cation *(2)* is about 23 kcal/mol more stable than *(3)*. An upper limit of the activation energy for transformation of *(3)* into *(2)* was calculated as 9 kcal/mol[2]. For comparison, the exper-

Table 1. Calculated structural data for cations *(2)* and *(3)* and radicals *(2')* and *(3')*. Bond lengths in Å, angles in °.

	(2)	*(2')*	*(3)*	*(3')*
C^1C^{10}	1.542	1.552	1.525	1.543
C^1C^2	1.445	1.453	1.525	1.520
C^2C^3	1.377	1.380	1.353	1.352
C^3C^4	1.515	1.518	1.525	1.520
C^4C^5	1.522	1.519	1.525	1.520
C^5C^6	1.352	1.352	1.353	1.352
C^4C^{10}	1.576	1.574	1.525	1.543
C^1H	—	—	1.118	1.122
C^2H	1.097	1.101	1.099	1.102
C^3H	1.103	1.101	1.099	1.102
C^4H	1.118	1.123	1.118	1.122
C^5H	1.099	1.102	1.099	1.102
$C^{10}H$	1.113	1.117	—	—
$C^2C^1C^{10}$	109.9	106.9	98.7	101.1
$C^2C^1C^9$	137.0	134.4	125.6	122.8
$C^1C^{10}C^4$	103.1	104.8	115.1	111.4
$C^4C^{10}C^7$	110.4	109.7	115.1	111.4
$C^1C^2C^3$	107.2	110.2	113.6	113.2
Calculated symmetry	C_s	C_s	C_{3v}	C_{3v}

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imentally determined activation energy for the 1,2 hydride shift on the 2-norbornyl cation is 10 kcal/mol[3].

These relative energy predictions have now been confirmed experimentally[4]. The calculated flattening of the carbenium ion into an almost planar divinylcarbenium ion is supported by the ^{1}H- and ^{13}C-NMR spectra[4].

Calculation with a UHF open-shell version of MINDO/3[5] shows the same stability sequence for the radicals *(2')* and *(3')*: Radical *(2')* is about 10.5 kcal/mol more stable than *(3')*. The calculated structural data are also listed in Table 1.

The stabilization of *(2)* by interaction with the conjugated double bonds is consistent with expectation. The optimized structure shows a marked shortening of the C^1C^2 and C^1C^9 bond lengths; the positive charge is distributed over the pentadienyl system.

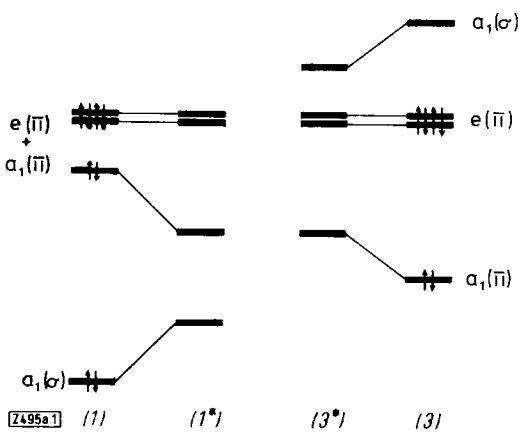

Fig. 1. Qualitative σ-π interaction diagram for triquinacene *(1)* and the 10-triquinacenyl cation *(3)*.

Generation of the cation *(3)* from *(1)* is likewise favored. This is due to σ-π interaction. The explanation is shown in Figure 1, where the relevant σ and π orbitals in *(1)* and *(3)* are compared with those of the corresponding models *(1*)* and *(3*)* without σ-π interaction. It is known that interaction between the two occupied orbitals $a_1(\sigma)$ and $a_1(\pi)$ in *(1)* leads to destabilization of the molecule[6]. On the other hand, interaction between the low-lying unoccupied orbital $a_1(\sigma)$ and the occupied orbital $a_1(\pi)$ in *(3)* must lead to stabilization of the cation. Analogous arguments apply in the case of radicals *(2')* and *(3')*. Accordingly, both the heterolytic and the homolytic cleavage of the $C^{10}H$ bond are accelerated by σ-π interaction.

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(1), 6053-74-3; *(2)*, 59983-40-3; *(2')*, 59983-41-4; *(3)*, 59983-42-5; *(3')*, 59983-43-6

[1] *R. C. Bingham, M. J. S. Dewar,* and *D. H. Lo,* J. Am. Chem. Soc. *97*, 1285 (1975).
[2] For calculation of the reaction route from *(3)* to *(2)*, C_s symmetry was assumed.
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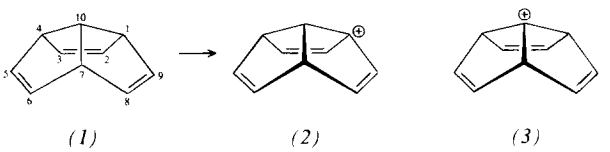
[5] *P. Bischof,* J. Am. Chem. Soc., in press.
[6] This interaction was detected photoelectron spectroscopically: *J. C. Bünzli, D. C. Frost,* and *L. Weiler,* Tetrahedron Lett. *1973*, 1159; *P. Bischof, D. Bosse, R. Gleiter, M. J. Kukla, A. de Meijere,* and *A. L. Paquette,* Chem. Ber. *108*, 1218 (1975).

Bridgehead Cations of Tricyclo[5.2.1.0^{4,10}]deca-2,5,8-triene (Triquinacene)[**]

By *Dieter Bosse* and *Armin de Meijere*[*]

Carbenium ion centers on both types of bridgehead positions of triquinacene *(1)*[1] ought, in contrast to a comparable system without double bonds, to be stabilized by interaction of the vacant bridgehead orbitals with the π orbitals of the double bonds. As the structural data of *(1)*[2] show, the 1-triquinacenyl cation *(2)* should be a twofold allyl-stabilized bridgehead cation. Semiempirical calculations[3] confirm this; moreover, they show that the 10-triquinacenyl cation *(3)* ought to be stabilized too, albeit to a lesser extent.

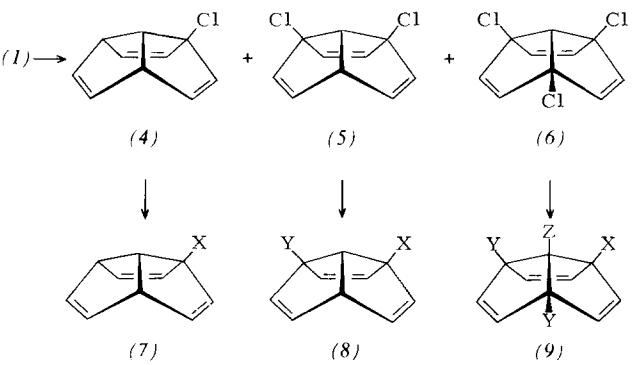


(1) *(2)* *(3)*

We have therefore investigated the possibilities of generating the bridgehead carbenium ions of *(1)*.

Photochlorination of *(1)* with *tert*-butyl hypochlorite at −50°C in trichlorofluoromethane (Frigen 11) affords a mixture of 1-chloro- *(4)*, 1,4-dichloro- *(5)*, and 1,4,7-trichlorotriquinacene *(6)*. The relative yields of *(4)*, *(5)*, and *(6)* can be varied by altering the ratio *(1)* : *tert*-butyl hypochlorite. On using a 3.6 molar excess the trichloride *(6)* was formed in *ca.* 75% yield and could be obtained pure by recrystallization[4]. *(4)* and *(5)* were isolated by preparative gas chromatography[4]. 10-chlorotriquinacene could not be detected in the product mixture.

(4) is sensitive to heat and light: in 80% dioxane/water it is completely hydrolyzed within 30 min at room temperature to 1-triquinacenol *(7a)*[4]; methanolysis leads to *(7b)*, reacence of sodium methoxide, *(5)* and *(6)* can also be converted tion with dimethylamine to *(7c)*[4]. In methanol in the presinto the methyl ethers *(8b)*[4] and *(9b)*[4], respectively. While *(5)* is completely hydrolyzed to the dialcohol *(8)*[4] within



(4) *(5)* *(6)*

(7) *(8)* *(9)*

(a), X, Y = OH; *(b)*, X, Y = OCH_3, Z = H; *(c)*, X = $N(CH_3)_2$; *(d)*, X = ⊕, Y = Cl, Z = H; *(e)*, X, Y = OCD_3, Z = D

5 h in boiling dioxane/water, *(6)* remains unchanged even after 72 h under the same conditions. This difference in behavior of *(6)* on hydrolysis and methanolysis can only be interpreted in terms of an elimination-addition mechanism[5], for reaction with [D_4]-methanol/sodium methoxide affords exclusively 10-deuterio-1,4,7-tris(trideuteriomethoxy)triquinacene

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Table 1. ^{1}H- and ^{13}C-NMR data of the triquinacenyl cations at −70 °C.

	^{1}H-NMR (τ) in SO_2ClF			^{13}C-NMR (δ) in SO_2ClF [a]		
	(7d) ≡ *(2)*	*(8d)*	*(9d)*	*(7d)* ≡ *(2)*	*(8d)*	*(9d)*
Pentadienyl unit	0.95 (A-part; H^3, H^8)	1.02 (A-part; H^8)		252.97 (C^1)	243.68 (C^1)	237.03 (C^1)
		1.43 (A-part; H^3)	1.50 (A-part; H^3, H^8)	195.15 (C^3, C^8)	195.61 (C^8)	
	2.13 (B-part; H^2, H^9)	2.04 (B-part; H^2)	2.00 (B-part; H^2, H^9)		183.28 (C^3)	183.92 (C^3, C^8)
	of an AB system	2.06 (B-part; H^9)		137.86 (C^2, C^9)	138.70 (C^9)	
		of an AB system			138.42 (C^2)	132.38 (C^2, C^9)
Olefinic positions	4.17 (s, H^5, H^6)	3.99 (A-part; H^5)	4.00 (s, H^5, H^6)	134.33 (C^5, C^6)	132.69 (C^5)	132.28 (C^5, C^6)
		4.19 (B-part; H^6)			133.83 (C^6)	
Central bridgehead position	4.48 (m, H^{10})	4.38 (d, H^{10})	4.40 (s, H^{10})	77.67 (C^{10})	84.55 (C^{10})	91.69 (C^{10})
Allylic positions	5.46 (m, H^4, H^7)	5.22 (m, H^7)		56.48 (C^4, C^7)	56.46 (C^7)	72.29 (C^4, C^7)
					73.61 (C^4)	

[a] Relative to tetramethylsilane.

(9e). A "dehydrotriquinacene"[6] (tricyclo[5.2.1.$0^{4,10}$]deca-1(10),2,5,8-tetraene and/or tricyclo[5.2.1.$0^{4,10}$]deca-1(2),3,5,8-tetraene) must occur as an intermediate; the chlorides *(4)*, *(5)*, *(6)*, and especially the dimethylaminotriquinacene *(7c)*, may be considered as potential precursors of this class of compounds.

For the generation and investigation of free carbocations of the triquinacene system all three chlorides *(4)*, *(5)*, and *(6)* were allowed to react with antimony pentafluoride in sulfuryl chloride fluoride at −78 °C and the ^{1}H- and ^{13}C-NMR spectra of the reaction mixture were recorded (see Table 1). According to these, only the monocations *(7d)* [≡ *(2)*], *(8d)*, and *(9d)*, respectively, were present in each case. Their kinetic stability increases with increasing chlorine substitution; thus *(7d)* already decomposes at −40 °C, whereas *(9d)* is still detectable spectroscopically even after 15 min at 25 °C. Trapping experiments with sodium methoxide in methanol led to the methyl ethers *(7b)*, *(8b)*, and *(9b)*, respectively, in good yields.

The ^{1}H- and ^{13}C-NMR spectroscopic data of the free carbenium ions show that almost planar divinylcarbenium ion units are present in these species. Increasing chlorine substitution in *(8d)* and *(9d)* leads to a lowering of the electron deficit in the divinylcarbenium ion units and thus to high-field shifts of the ^{1}H- and ^{13}C-NMR signals.

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[1] *T. Jacobsen*, Acta Chem. Scand. *21*, 2235 (1967); *C. Mercier*, *P. Soucy*, *W. Rosen*, and *P. Deslongchamps*, Synth. Commun. *3*, 161 (1973).

[2] *E. D. Stevens*, *J. D. Kramer*, and *L. A. Paquette*, J. Org. Chem. *41*, 2266 (1976).

[3] *P. Bischof*, Angew. Chem. *88*, 609 (1976); Angew. Chem. Int. Ed. Engl. *15*, 556 (1976).

[4] The ^{1}H-NMR, ^{13}C-NMR, and mass spectra as well as elemental analysis of all the new compounds are in agreement with the given structures.

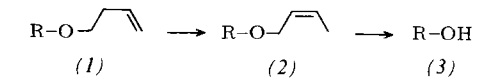
[5] See also: *K. B. Wiberg*, *R. K. Barnes*, and *I. Albin*, J. Am. Chem. Soc. 79, 4994 (1957).

[6] A perchlorotricyclo[5.2.1.$0^{4,10}$]deca-1(10),2,5,8-tetraene was detected by *T. Jacobsen*, Chem. Scr. 5, 174 (1974).

Cleavage of Allyl Ethers with Pd/C[**]

By *Roland Boss* and *Rolf Scheffold*[*]

Allyl ethers *(1)* are to a large extent stable under basic and acid conditions. Because of this property the allyl group is often used as protecting group for alcohols. Removal of the protecting group is usually effected by isomerization of the allyl ether to the corresponding enol ether *(2)* with subsequent H^+ or Hg^{2+}[1] catalyzed hydrolysis or oxidative cleavage[2].



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

Since the known methods[3] for allyl ether cleavage did not lead to the alcohol *(9a)* in the case of the glycidonitrile allyl ether *(9)* we investigated the heterogeneously catalyzed isomerization of allyl ethers to *cis*-enol ethers. We found palladium/activated charcoal to be a particularly suitable catalyst for this purpose[4].

If isomerization is carried out under conditions favoring hydrolysis of the *cis*-enol ethers the cleavage products alcohol and propionaldehyde are obtained directly. Since both the catalyst as well as the propionaldehyde (b.p. 49 °C) can be separated very easily this allyl ether cleavage is very useful (cf. examples in Table 1). That the allyl protecting group can be selectively removed besides other protecting groups is illustrated by the examples glycerol 1-allyl 2,3-dibenzyl ether *(7)*.

The allyl ether to be cleaved is heated for a few hours at 60° to 80 °C in a mixed solvent (see Table 1) in the presence of a trace of *p*-toluenesulfonic acid or mineral acid (*e.g.* perchloric acid) and a catalytic amount of palladium on activated charcoal[5]. In the case of sensitive substrates, *e.g.* the glycidonitrile *(9)*, the cleavage can be carried out over a prolonged period of time (up to *ca.* 6 days) at room temperature.

Using this method 2,5-dihydrofuran can be cleaved smoothly in methanol/water to 4-hydroxybutanol, while 3-methoxycyclohexene remains unchanged under comparable conditions. This finding would suggest that a cisoid conformation of the allyl ether partial structure is a prerequisite for the palladium-catalyzed isomerization[3].

Experimental

Glycerol 1,2-dibenzyl ether *(7a)*: A solution of *(7)* (1.00 g, 3.2 mmol) in methanol (10 ml) and water (2 ml) is treated with palladium/activated charcoal (0.1 g) and toluenesulfonic acid (0.1 g). The resulting suspension is boiled under reflux with stirring for 24 hours. After removal of catalyst by centrifugation the solution is extracted with ether, the solvent removed in a rotary evaporator, and the residue distilled. The yield of *(7a)* (b.p. 150 °C/0.05 torr[2]) is 0.85 g (97 %).

Methyl 2-(4-hydroxymethyl-2-methoxy-6-oxo-4-vinyl-1-cyclohexenyl)acrylate *(8a)*: To a solution of *(8)* (3.9 g, 13.3 mmol) in anhydrous methanol (170 ml) is added palladium/

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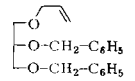
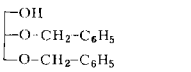
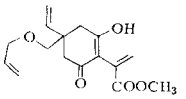
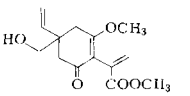
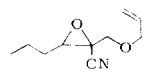
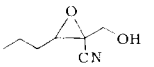
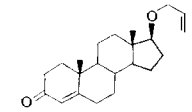
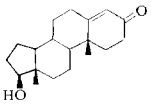
Table 1. Converted allyl ethers.

Allyl ether	Reaction conditions [a]	Product	Yield [%] [b]
(4) C_6H_5–O–	Pd/C methanol/H_2O/H^+ 6 h reflux	(4a) C_6H_5–OH	>95
(5) n-C_8H_{17}–O–	Pd/C methanol/H_2O/H^+ 6 h reflux	(5a) n-C_8H_{17}–OH	>95
(6)	Pd/C H_2O/H^+ 6 h 80 °C	(6a)	>95
(7) 	Pd/C methanol/H_2O/H^+ 24 h reflux	(7a) 	>95
(8) 	Pd/C anhydrous methanol/TsOH 20 h reflux	(8a) 	84
(9) 	Pd/C dioxane/H_2O/H^+ 6 days room temperature	(9a) 	78
(10) 	Pd/C ethanol/H_2O/H^+ 3 h reflux	(10a) 	84

[a] Where not stated otherwise perchloric acid in concentrations of 1 to 5 mmol/ether was used as acid (H^+).
[b] The yields refer to isolated material.

activated charcoal (0.6 g) and *p*-toluenesulfonic acid (0.3 g) and the stirred suspension boiled under reflux for 20 hours. After removal of the catalyst by filtration, the filtrate is concentrated to half its original volume in a rotary evaporator, treated with saturated NaCl solution and ice, and extraced five times with dichloromethane. After removal of solvent in a rotary evaporator there remains a pale yellow oil which crystallizes on drying in a high vacuum. Melting point after a single recrystallization from ether: 87 to 89 °C. Yield 3.0 g (84 %).

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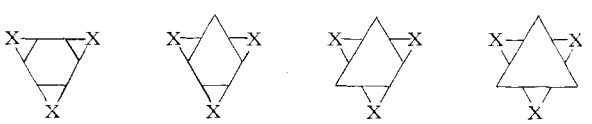
(4), 1746-13-0; *(4a)*, 108-95-2; *(5)*, 3295-97-4; *(5a)*, 111-87-5; *(6)*, 123-34-2; *(6a)*, 56-87-5; *(7)*, 59991-88-7; *(7a)*, 59991-89-8; *(8)*, 59991-90-1; *(8a)*, 59991-91-2; *(9)*, 59991-92-3; *(9a)*, 59991-93-4; *(10)*, 20860-14-4; *(10a)*, 58-22-0; palladium 7440-05-3

[1] *R. Gigg* and *C. D. Warren*, J. Chem. Soc. *C 1968*, 1903.
[2] *J. Cunningham*, *R. Gigg*, and *C. D. Warren*, Tetrahedron Lett. *1964*, 1191.
[3] *T. J. Prosser*, J. Am. Chem. Soc. *83*, 1701 (1961); *C. C. Price* and *W. H. Snyder*, *ibid. 83*, 1773 (1961); *H. C. Clark* and *H. Kurosawa*, Inorg. Chem. *12*, 357, 1566 (1973); *E. J. Corey* and *J. W. Suggs*, J. Org. Chem. *38*, 3224 (1973).
[4] We used the hydrogenation catalyst 10 % palladium on activated charcoal obtainable from Fluka. Experiments with rhodium on activated charcoal also gave positive results; ruthenium and platinum on activated charcoal proved less useful. This is in agreement with the finding that palladium proves to have the greatest tendency for shifting double bonds in hydrogenations. Cf. also *P. N. Rylander*, Adv. Chem. Ser. *98*, 150 (1971).
[5] As is to be expected the allyl cleavage is blocked by traces of "catalyst poisons" such as thiophenol and potassium cyanide. It is therefore recommended that the reaction vessel be cleaned with chromic sulfuric acid, washed with potassium hydroxide solution, and finally rinsed with demineralized water.

Synthesis of *cis*-Trioxa-tris-σ-homotropilidene[**]

By *Horst Prinzbach* and *Christoph Rücker*[*]

Preparative and mechanistic objectives stimulated extension of our work on the tris-σ-homobenzenes *(1)* (X = CR_2, O, NR, S)[1] to investigation of the homologs *(2)*—*(4)*. After having recently described the first valence isomeric σ/π-hexahomobenzenes *(4)*[2], we now report the dioxa-bis- and trioxa-tris-σ-homotropilidenes *(2)* (X = O)[3].



(1) *(2)* *(3)* *(4)*

Mainly because of our particular interest in the stereoelectronic features of valence isomerization in the *cis*-trioxide *(10)*, we have commenced our study program in this area with an investigation of the chances and stereoselectivity of a stepwise epoxidation of tropilidene. On reaction of excess peroxy acid (peroxyacetic acid, *m*-chloroperoxybenzoic acid) with the readily accessible oxide *(5)*[4] in dichloromethane/Na_2CO_3 the four dioxides *(6)*—*(9)* are formed, whereby the dioxide *(6)* is, according to a capillary-GC/MS analysis, the least favored product (total yield of products up to 40 %, ratio in a typical experiment *ca.* 6:26:27:41). Preparative gas chromatography affords pure *(7)* and a mixture of *(8)*/*(9)*

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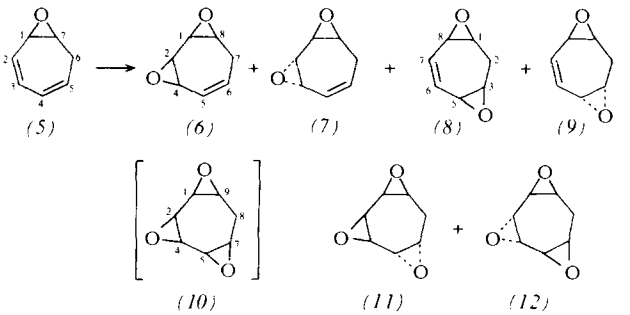
($\tau_{2(2')\text{-H}}=7.7$ and $\tau_{2\text{-H}}=8.7$, $\tau_{2'\text{-H}}=7.2$, respectively). Epoxidation of *(6)* through *(9)*, however, is achievable only under very drastic conditions [*m*-chloroperoxybenzoic acid, boiling 1,2-dichloroethane (b.p. 83°C), 2,6-di-*tert*-butylphenol[5]]; accordingly, the proportion of by-products and loss of oxidizing agent are high.



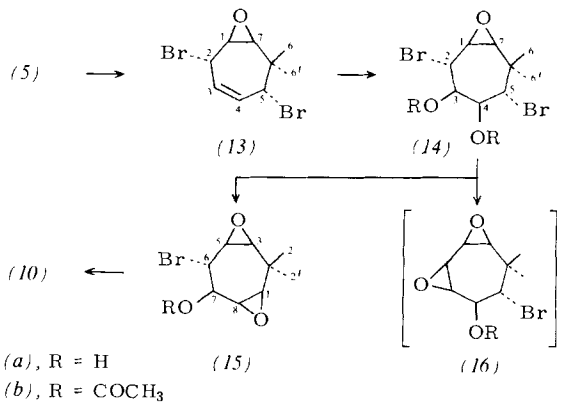
(5) *(6)* *(7)* *(8)* *(9)*

(10) *(11)* *(12)*

The two trioxides identified by GC/MS analysis of the complex reaction mixture and isolated in very small amounts as a mixture (*ca.* 1:1) are confirmed as being *(11)* and *(12)*, respectively, by their ^{13}C-data [$CDCl_3$, $\delta=53.2$ ppm, 52.9, 52.5, 52.4, 51.4, 50.7, 27.4 (C-8) and $\delta=52.1$ ppm, 50.9, 50.4, 32.5 (C-8), respectively]. Accordingly, this serves as a preparatively useful route to *(7)* and, with limitations—considerable problems exist regarding separation—also to *(8)* and *(9)*, but not to compounds *(10)*—*(12)*.

We have found a route—based on the synthesis of the trioxide *(1)* (X=O)[6]—to the compound *(10)* undetectable direct oxidation of *(5)*, namely the reaction sequence *(5)* → *(13)* → *(14)* → *(15)*/*(16)* → *(10)*. The critical *anti-cis*-1,4 addition of bromine to *(5)* can be accomplished—albeit with not yet optimized regio- and stereospecificity (65%)—in Na_2CO_3-buffered dichloromethane solution at −78°C; chromatographically [silica gel, benzene/cyclohexane (1:1), 0°C] purified *(13)* (m.p. 51°C) is stable in solution below −60°C, but is slowly converted into an isomeric mixture at higher temperatures. The *anti*-2,5 position of the Br residues follows, above all, from the ^{1}H-NMR data (Table 1). The *cis*-hydroxylation *(13)* → *(14a)* with potassium permanganate at 0°C (acetone/water, $MgSO_4$) is still impaired by the partial isomerization of *(13)*; the crystalline diol (m.p. 130°C) isolated in yields of 35% to 45% was analyzed ^{1}H-NMR spectroscopically as diacetate *(14b)* (m.p. 148—149°C). On the basis of the coupling parameters (Table 1) twist-like conformations with quasi-equatorial arrangement of the residues on C-2, C-3 and quasi-axial arrangement of those on C-4,'C-5 are most likely for *(14a)*/*(14b)*. The twofold epoxide formation *(14a)* → *(10)* with three equivalents of potassium methoxide (MeOH, THF) proceeds without noticeable competition at 20°C. Chromatography (DC) and ^{1}H-NMR spectrometry reveal only one intermediate which has limited kinetic stability under the given conditions. The product isolated in very small amounts along with *(14)* and *(10)* on using only one equivalent of base is the non-crystalline *(15a)*, which was converted into the crystalline acetate *(15b)* (m.p. 137°C) in the conventional way. The preferred formation of *(15)* was to be expected on account of the steric conditions in *(14)*, without us so far being able to definitely rule out *(16)* as a further intermediate.

The structure of the *cis*-trioxide *(10)* (colorless crystals, m.p. 165°C, yield >90%, not optimized) is confirmed by the stereochemistry of its precursors and by its spectral data. On the basis of the comparable magnitude of $J_{7,8}$ ($J_{8,9}$) and $J_{7,8'}$ ($J_{8',9}$) *(10)* ought to be present as cisoid *(10a)*, and not as the transoid boat *(10b)*, less plausible because of transannular interactions. For both conformations, with a



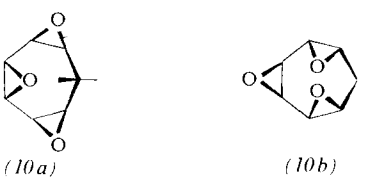
(5) → *(13)* → *(14)* (OR) → *(16)* → *(10)* ← *(15)*

(a), R = H
(b), R = $COCH_3$

Table 1. H—H coupling constants [cps] of compounds *(7)*, *(10)*, *(13)*, *(14b)*, and *(15b)*.

(7)	$J_{1,2}<1$, $J_{2,4}=4$, $J_{5,6}=11$, $J_{7,7'}=15$
(10)	$J_{1,2}\leq 1.5$, $J_{7,8}\approx 8$, $J_{7,8}\approx 6$, $J_{8,8'}=14$
(13)	$J_{1,2}=4.5$, $J_{1,7}=4.5$, $J_{2,3}=4.5$, $J_{3,4}=12$, $J_{4,5}\approx 3$, $J_{5,6}=3.8$, $J_{5,6'}=9.8$, $J_{6,6'}=15$, $J_{6,7}=6.8$, $J_{6',7}=2.3$
(14b)	$J_{1,2}=6.8$, $J_{1,7}=4.5$, $J_{2,3}=10.5$, $J_{3,4}=2.3$, $J_{4,5}=5.4$, $J_{5,6}=1.5$, $J_{5,6'}=6.0$, $J_{6,7}\approx 6$, $J_{6',7}\approx 5$, $J_{6,6'}=15$
(15b)	$J_{1,2'}\approx J_{2',3}=6.8$, $J_{2,2'}=16$, $J_{5,6}=7.5$, $J_{6,7}=12$, $J_{7,8}=3$

HC(1)—C(2)—H torsion angle of 20 to 40°[7] a ^3J coupling constant of 2—3 cps can be expected, so this criterion does not allow a decision between *(10a)* and *(10b)* or—other than in the case of the *cis*/*trans* trioxides *(1)* (X=O)[8]—between *(10)* and *(12)* (torsion angle *ca.* 90°; $J\leq 1$ cps).



(10a) *(10b)*

The structures of the new compounds are also confirmed by elemental analysis, MS, ^{13}C-NMR and IR data, and that of *(10)* in particular by various chemical transformations[9].

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(5), 33250-14-5; *(10)*, 59992-00-6; *(13)*, 59992-01-7; *(14a)*, 59992-02-8; *(14b)*, 59992-03-9; *(15b)*, 59992-04-0

[1] *H. Prinzbach, D. Stusche, J. Markert,* and *K.-H. Limbach,* Chem. Ber. *1976*, in press, and literature cited therein.
[2] *H. Prinzbach, V. Wessely,* and *H. Fritz,* Tetrahedron Lett. *1976*, 2765.
[3] In the meantime we have obtained a trioxide *(3)* (X=O) whose configuration is still unknown.
[4] *P. Schiess* and *M. Wisson,* Helv. Chim. Acta *57*, 980 (1974).
[5] *Y. Kishi, M. Aratani, H. Tanino, T. Fukuyama, T. Goto, S. Inoue, S. Sugiura,* and *H. Kakoi,* J. Chem. Soc. Chem. Commun. *1972*, 64.
[6] *R. Schwesinger* and *H. Prinzbach,* Angew. Chem. *84*, 990 (1972); Angew. Chem. Int. Ed. Engl. *11*, 942 (1972); *E. Vogel, H.-J. Altenbach* and *C. D. Sommerfeld, ibid. 84*, 986 (1972) and *11*, 939 (1972).
[7] A derivative of *(2)* (X=N—Ac, X=CH_2) [1] confirmed by X-ray structure analysis as *cis*-aza-tris-σ-homotropilidene (Dr. *C. Krüger*, Max-Planck-Institut für Kohlenforschung, Mülheim/Ruhr) is a cisoid boat with corresponding torsion angles of 40.5° and 38.3°.
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[9] *Note added in proof* (August 16, 1976): The cisoid boat structure *(10a)* has in the meantime been confirmed by X-ray structure analysis (Dr. *C. Krüger*).

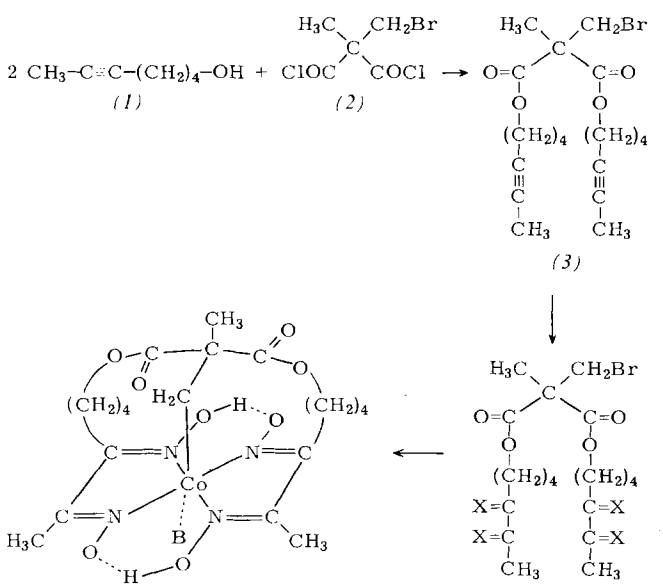
Synthesis, Structure Determination, and Rearrangement of a Model for the Active Site of Methylmalonyl-CoA Mutase with Incorporated Substrate[**]

By *Helmut Flohr*, *Wolfgang Pannhorst*, and *János Rétey*[*]

Dedicated to Professor Vladimir Prelog on the occasion of his 70th birthday

It has recently been shown by us[1] and by others[2] that a malonic ester substituted in the β-position with cobalt can rearrange into the corresponding succinic ester. Although a chemically analogous case for the enzyme-catalyzed isomerization of methylmalonyl-CoA to succinyl-CoA has thus been found, this model is in many respects not in keeping with the conditions at the active site of the enzyme. Soon after homolytic cleavage of the cobalt-carbon bond the malonic ester "substrate" loses contact with the central cobalt atom and, thus deprived of that atom's catalytic effect, is no longer able to rearrange[3]. This could explain the low[2] and variable[1] yields of rearrangement product. In order to better simulate the situation on the enzyme, we synthesized a cobalt complex in which the "substrate" is anchored covalently by two methylene bridges to a planar part of the complex.

5-Heptyn-1-ol *(1)*[4, 7] was reacted with 2-bromomethyl-2-methylmalonic acid dichloride *(2)* to give the diester *(3)*, which on treatment with ozone at −18 °C[5, 7] yielded the crude tetraketone *(4)*. The tetraoxime *(5)* obtained from *(4)* in 80% yield [referred to *(3)*] was finally allowed to react in dilute ethanolic solution with a stoichiometric amount of cobalt(II) chloride, twice the amount of pyridine, three equivalents of potassium hydroxide, and excess $NaBH_4$. Alkylated cobalt complexes were isolated from the mixture in 17% yield [referred to *(5)*]. Subsequent thin-layer chromatographic separation and recrystallization from acetone/water (with 1% pyridine) afforded the major product *(6)* in pure form in 7% yield [referred to *(5)*]. $R_f = 0.44$, chloroform : isopropanol : pyridine = 94 : 5 : 1, Macherey-Nagel plates, SILG-25-UV$_{254}$.



(6), B = Pyridine
(7), B = Methanol

(4), X = O
(5), X = NOH

Comparison of the ^{1}H-NMR[6] and UV spectra with those of known cobaloximes[1, 7] revealed without doubt that the product was the intramolecularly alkylated cobalt complex *(6)*.

Irradiation of a methanolic solution of *(6)* with a mercury high-pressure lamp for 60 min in the absence of oxygen led to replacement of the pyridine ligand by methanol. Thin-layer chromatography of the photoproduct (chloroform: isopropanol = 95:5, $R_f = 0.11$; hexane : isopropanol : methanol = 5 : 2 : 1, $R_f = 0.11$) afforded the cobaloxime *(7)*.

(7) crystallizes from CD_3OD in the space group $P\bar{1}$ with $a = 11.090$, $b = 13.772$, $c = 8.971$ Å; $\alpha = 99.75$, $\beta = 119.49$, $\gamma = 84.83°$; $Z = 2$. A total of 3076 symmetrically independent reflections were measured on a Picker diffractometer (MoK_z radiation), of which 2269 were classified as observed. The positions of the Co atoms were determined by a Patterson synthesis, the positions of all the other atoms other than hydrogen by difference Fourier syntheses. Refinement of the atomic coordinates and the anisotropic temperature factor coefficients for atoms other than hydrogen converged at $R = 0.056$.

Cobaloxime *(7)* adopts in the crystal lattice a chiral conformation; the ester carbonyl groups of the bridges point in opposite directions. The methyl group in the bridge center (on C-10) projects away from the plane of the equatorial ligands. The angle Co—C20—C'10 is 127.5°, compared with 125° and 117.3° for the corresponding angles in coenzyme B_{12}[8] and in methylene-bridged cobaloxime[7], respectively.

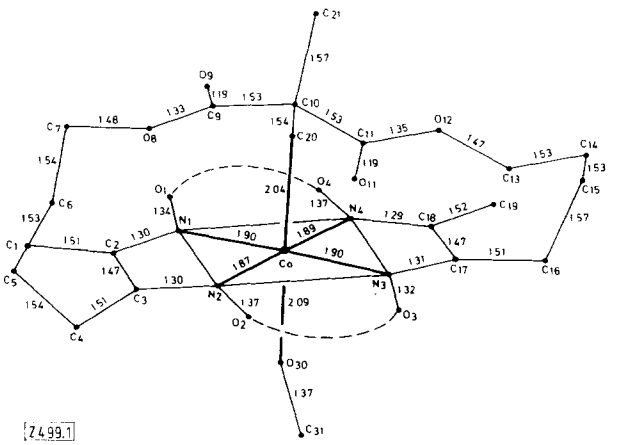


Fig. 1. Structure of the cobaloxime *(7)*. Lengths given in Å.

A solution of *(6)* (16 mg) in anhydrous methanol (15 ml) was purged repeatedly with nitrogen. The cooled solution (*ca.* 15 °C) was then irradiated with a mercury high-pressure lamp (125 W, Phillips) from a distance of 5 cm. Thin-layer chromatographic monitoring of the reaction showed that all Co-alkyl bonds were cleaved after 12 hours. After hydrolysis with excess ethanolic potassium hydroxide the solvent was removed *in vacuo*, the residue treated with 2 ml 1 N HCl and continuously extracted with ether. Thin-layer chromatographic investigation showed that the ether extract contained methylsuccinic acid as the sole organic acid. In particular, no dimethylmalonic acid could be detected. Thin-layer chromatography of the crude product (chloroform : glacial acetic acid = 5:1, $R_f = 0.47$, and diisopropyl ether: formic acid: water = 90:7:3, $R_f = 0.61$) afforded crystalline methylsuccinic

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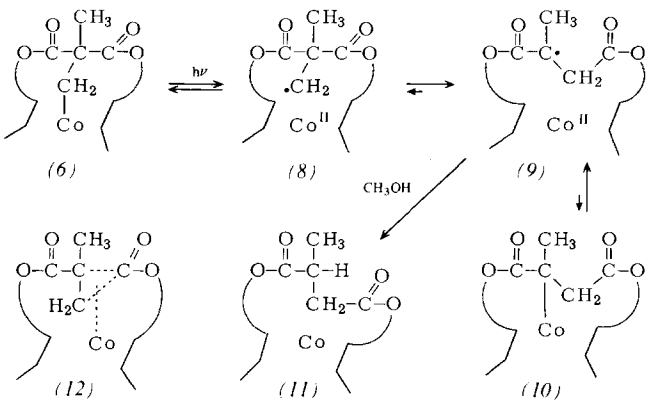
acid (m.p. 105—108 °C, ^{1}H-NMR and IR spectra identical with those of an authentic sample) in 82% yield (3 mg).

We explain the above results as follows: The light-induced homolysis of the cobalt-carbon bond leads to the radical *(8)*, which with participation of the cobalt rearranges reversibly into the radical *(9)*. Recombination in *(9)* would lead to the unstable *tert*-alkylcobaloxime *(10)*[9]. Of the species *(8)*, *(9)* and *(10)*, which are in equilibrium with each other, *(9)* has the highest population and can be stabilized to *(11)* by irreversible H-abstraction from the solvent. For radical *(8)* this reaction cannot compete with that of the intramolecular recombination leading to the stable *(6)*. The rearrangement might start from the radical species *(8)* or *(9)*; however a cobalt-stabilized intermediate *(12)* which could break down either to *(8)* or *(9)* would also be plausible.



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CAS Registry numbers:
(1), 58944-42-6; *(2)*, 60004-35-5; *(3)*, 60004-36-6; *(4)*, 60004-37-7; *(5)*, 60004-38-8; *(6)*, 60064-54-2; *(7)*, 60064-55-3; *(11)*, 60118-01-6; methylmalonyl-CoA mutase, 9023-90-9

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[2] *P. Dowd* and *M. Shapiro*, J. Am. Chem. Soc. *98*, 3724 (1976).
[3] *S. N. Lewis, J. J. Miller*, and *S. Winstein*, J. Org. Chem. *37*, 1478 (1972); *G. Bidlingmaier* and *J. Rétey*, unpublished work: reaction of 2-bromomethyl-2-methylpropanediacid diethyl ester[1] with tri-*n*-butyltin hydride gave exclusively 2,2-dimetbylpropanediacid diethyl ester.
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[5] *L. Ré, B. Maurer* and *G. Ohloff*, Helv. Chim. Acta *56*, 1882 (1973).
[6] We are grateful to *T. Keller, V. Formaček*, and Dr. *W. E. Hull* (Bruker Physik, Karlsruhe) for recording the ^{1}H-NMR spectra with the WH-270-MHz spectrometer.
[7] *H. Flohr, U. M. Kempe, W. Pannhorst*, and *J. Rétey*, Angew. Chem. *88*, 443 (1976); Angew. Chem. Int. Ed. Engl. *15*, 427 (1976).
[8] *P. G. Lenhert* and *D. Crowfoot-Hodgkin*, Nature *192*, 937 (1961); *P. G. Lenhert*, Proc. Roy. Soc. *A 303*, 45 (1968).
[9] Attempts to synthesize cobaloxime *(10)* directly from the ligand prepared analogously to *(5)* have so far failed.

Structure and Density Distribution of Bonding Electrons of Cumulenes[**]

By *Hermann Irngartinger* and *Hans-Ulrich Jäger*[*]

We have determined the structures of the cumulenes *(1)* and *(2)*[1] at room temperature and carried out low-temperature measurements for ascertaining the density distribution of bonding electrons in hexapentaene *(1)*[2]. For *(1)* and *(2)* the measurements at room temperature (MoK_α radiation; graphite monochromator; $\sin\theta/\lambda \leq 0.66$) gave R values of 0.067 and 0.064, respectively, after refinement with all reflections. The crystallographic data are listed in Table 1. In the case of the triene *(2)* full 2/m molecular symmetry is preserved in the crystal, which to our knowledge has never been found previously in an organic compound in the solid state. The averaged bond lengths and angles (Fig. 1) are corrected to "rigid body motion".

Table 1. Crystallographic constants of *(1)* and *(2)*.

	(1)		*(2)*
22 °C		−165 °C	22 °C
a = 8.444(1) Å		8.253(1) Å	a = 14.485(2) Å
b = 11.536(2)		11.498(2)	b = 10.021(2)
c = 12.040(2)		11.756(1)	c = 13.576(2)
β = 114.91°(1)		113.94°(1)	
$P2_1/c$; Z = 2			Cmca; Z = 4
$D_{calc.}$ = 1.013		1.056	1.013 g·cm^{-3}

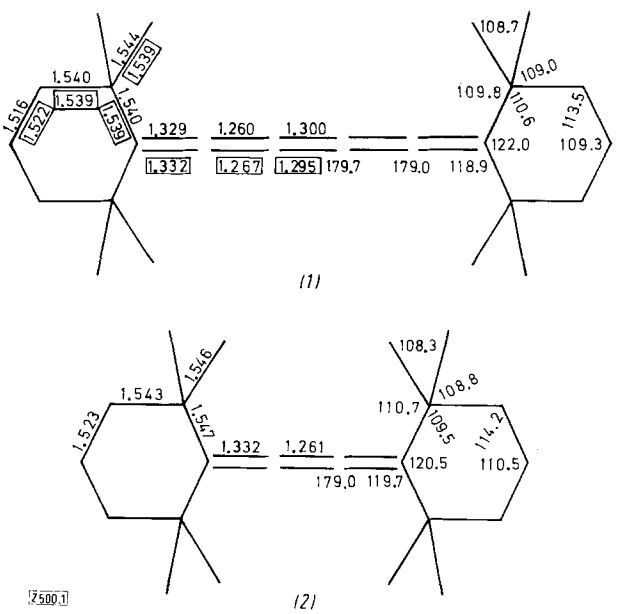

Fig. 1. Averaged bond lengths [Å] and angles [°] of 1,4-bis(2,2,6,6-tetramethylcyclohexylidene)butatriene *(1)* and 1,2-bis(2,2,6,6-tetramethylcyclohexylidene)ethylene *(2)*. The low-temperature values are framed.

From the bond angles it can be seen that the cumulene systems *(1)* and *(2)* are linear. The terminal C(sp^2)—C(sp) double bond of the triene system *(2)* with a value of 1.332 Å is slightly shorter than the standard value for a C(sp^2)—C(sp^2) double bond (1.34 Å). In *(2)* the central double bond situated between two sp-hybridized atoms is significantly shortened (1.261 Å). Similar differences in the double bonds have been found in unsubstituted butatriene[3] and in tetraphenylbutatriene[4]. The terminal double bonds in hexapentaene *(1)* are identical with the corresponding bonds in the butatriene *(2)*. The central C(sp)—C(sp) double bond with 1.300 Å, however, is longer than the neighboring bond of similar type. In contrast to the theoretically calculated bond lengths of 1.310 (terminal), 1.292, 1.292 Å (central)[5] for unsubstituted hexapentaene, our measurements indicate a clear alternation of bond lengths in the cumulene system of the hexapentaene *(1)*.

For determination of the electron density distribution in *(1)* four independent sets of reflections with a total of 28000 intensities were recorded at −165 °C up to $\sin\theta/\lambda \leq 1.2$ on

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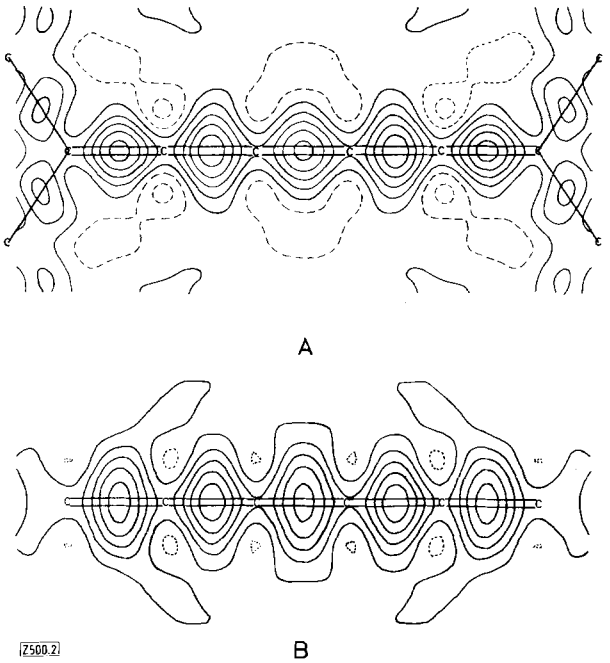

Fig. 2. Density distribution of bonding electrons in the cumulene system of *(1)* in a plane A, which contains the C atoms 2 and 6 of the cyclohexane ring, and a plane B perpendicular to A. The contour interval is 0.1 e/Å^3. Negative portions are drawn with dotted lines.

a computer-controlled Siemens diffractometer furnished with a Leybold-Heraeus low-temperature device[6]. After subsequent averaging of data, the refinement (C anisotropically, H isotropically) was carried out only with reflections of higher order in the range $0.7 \leq \sin\theta/\lambda \leq 1.2$ and yielded an R value of 0.04. The difference in density was computed from the atomic coordinates and temperature factors obtained using the set of data up to $\sin\theta/\lambda = 0.8$. The electron density distribution in the bonds of the cumulene system of *(1)* is depicted in Figure 2 for two sections perpendicular to each other along the cumulene axis. In section A, which contains the carbon atoms of the substituents, the bonding electron density of the second and fourth double bond is more strongly elongated vertical to the bond axis than in the neighboring double bonds, while in section B the elongation in the first, third and fifth double bond is strongest. The theoretical conceptions of the arrangement of π electrons in the double bonds of cumulated systems are thus in accord with our results.

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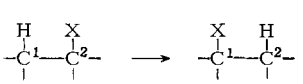
CAS Registry numbers:
(1), 60004-33-3; *(2)*, 60004-34-4

[1] Synthesis: *F. Bohlmann* and *K. Kieslich*, Chem. Ber. *87*, 1363 (1954).
[2] In connection with our investigations on the cumulenes, which were carried out in collaboration with *L. Leiserowitz*, Weizmann Institute of Science Rehovot (Israel) and *F. Nader* in our Institute.
[3] *O. Bastiansen* and *M. Traetteberg*, Tetrahedron *17*, 147 (1962).
[4] *Z. Berkovich-Yellin* and *L. Leiserowitz*, J. Am. Chem. Soc. *97*, 5627 (1975).
[5] *R. C. Bingham*, *M. J. S. Dewar*, and *D. H. Lo*, J. Am. Chem. Soc. *97*, 1294 (1975).
[6] *H. Dietrich*, Messtechnik *76*, 303 (1968).

ABSTRACTS

The vitamin B_{12} coenzyme forms the subject of a review by *R. H. Abeles* and *D. Dolphin*. Coenzyme B_{12} carries a covalently bound 5'-deoxy-5'-adenosyl group instead of the cyano group of the vitamin (cyanocobalamin); both compounds are cobalt(III) derivatives. Coenzyme B_{12} and a few alkylcobalamins are the only known organometal compounds in Nature. Ten enzymatic reactions are presently known in which the coenzyme B_{12} is needed as cofactor. Nine of these proceed according to the following scheme:



The review also deals with the hydrogen transfer step and with the mode of action of the coenzyme. [The Vitamin B_{12} Coenzyme. Acc. Chem. Res. *9*, 114—120 (1976); 57 References]

[Rd 869 IE—L]

New synthetic methods for monocyclic 1*H*-, 2*H*-, and 3*H*-pyrroles are described by *J. M. Patterson*. The synthesis of 1*H*-pyrroles from cyclic precursors involves ring substitution, substituent migration, elimination, rearrangement, ring expansion and ring contraction reactions. Available for the synthesis of 1*H*-pyrroles from acyclic precursors by ring closure are, *inter alia:* dicarbonyl compounds, unsaturated compounds such as dienes, nitriles, alkynes, and enamines as well as amino- and halocarbonyl compounds. 2*H*- and 3*H*-pyrroles are obtained by alkylation of 1*H*-pyrroles, thermal isomerization, photoisomerization, ring closure of suitably substituted precursors, and in an oxidative way (photo- or electrochemically). [Recent Synthetic Methods for Pyrroles and Pyrrolenines (2*H* or 3*H*-Pyrroles). Synthesis *1976*, 281—304; 242 references]

[Rd 871 IE—M]

The spectral, potentiometric, and energy-linked properties of cytochrome c oxidase in mitochondria are discussed by *M. K. H. Wikström*, *H. J. Harmon*, *W. J. Ingledew*, and *B. Chance* from new points of view. Contrary to the generally accepted hypothesis, cytochromes a and a_3 are not both responsible for the α-band at 605 nm; the band is in fact due only to cytochrome a. The two hemes of cytochrome oxidase take part in strong interaction with one another, which is expressed in the redox properties, the spin state, and the light absorption of the enzyme. The effect of ligands on cytochrome c oxidase is discussed on the basis of new knowledge; the consequences of the heme-heme interaction for the mode of action of the enzyme and its control by the energy state of the mitochon-

drion are particularly emphasized [A Re-Evaluation of the Spectral, Potentiometric and Energy-Linked Properties of Cytochrome c Oxidase in Mitochondria. FEBS Lett. *65*, 259—277 (1976); 59 references]

[Rd 875 IE—R]

The pathway of nitrogen assimilation in plants forms the subject of a paper by *B. J. Miflin* and *P. J. Lea*. In contrast to the long-held hypothesis that the main pathway is the reductive amination of α-ketoglutarate, recent investigations indicate that in the case of a deficiency of ammonia most bacteria take an alternative path *via* glutamine synthetase and glutamine-α-ketoglutarate aminotransferase (glutamate synthase). This aminotransferase is also found in higher plants and green and blue algae. The only exception is formed by the fungi. There are, therefore, grounds for the assumption that the assimilation of ammonia into amino-acid metabolism in plants and bacteria normally takes place through the glutamine synthetase—glutamate synthase pathway, while the route *via* glutamate dehydrogenase is chosen only when there is an excess of ammonia. [The Pathway of Nitrogen Assimilation in Plants. Phytochemistry *15*, 873—885 (1976); 148 references]

[Rd 877 IE—R]

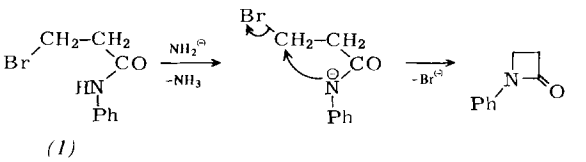
Plant constituents with potential anticancer and cytotoxic activity are discussed by *G. A. Cordell* and *N. R. Farnsworth*. The *Catharanthus* alkaloids vincaleukoblastin and leurocristin are of particular interest because of their antitumoral activity. Cytotoxic compounds from *Catharanthus* species belong to the β-anilinoacrylate group of indole alkaloids. In addition, representatives of these species show other pharmacological effects such as hypoglycemic or antiviral activity. The antitumoral principles of *Chelodonium majus* are sanguinarine and chelerythrine; chelidonine and protopine have cytotoxic effects. A promising group of benzophenanthridine alkaloids includes fagaronine (antitumoral activity) and the strongly cytotoxic nitidine. Cytotoxic compounds are present in Boehmeria species *(Urticaceae)*. Cryptopleurine displays antiviral and antitumoral activity. Both activities are also found in macrolide alkaloids, of which maytansine from *Maytenus senegalensis* is to be tested clinically in the near future. Of lignanes with antitumoral and cytotoxic activities, podophyllotoxin is singled out. A compound of relatively simple structure from *Jacaranda caucana*, jacaranone shows activity both *in vitro* and *in vivo*. The antitumoral activity of many plants is due to their tannin content. [A Review of Selected Potential Anticancer Plant Principles. Heterocycles *4*, 393—427; 100 references].

[Rd 878 IE—M]

The sesquiterpenes formed by Solanaceae under stress conditions are the subject of an article by *A. Stoessl*, *J. B. Stothers*, and *E. W. B. Ward*. The chemistry and some physical properties of these compounds are reviewed. Particular importance is attached to the ^{1}H- and ^{13}C-NMR spectra. The compounds are closely related to one another biogenetically. Their biological function may consist in protection of the plants against fungal infections. [Sesquiterpene Stress Compounds of the Solanaceae. Phytochemistry *15*, 855—872 (1976); 156 references].

[Rd 876 IE—R]

The synthesis of β-lactams (2-azetidinones) is considered by *N. S. Isaacs*. β-Lactams occur in Nature, *e.g.* in penicillins and cephalosporins. The four-membered ring system is accessible, *inter alia*, by cyclization of C_3N systems like *(1)*, by non-concerted cycloaddition, by [2+2] cycloaddition, by ring



(1)

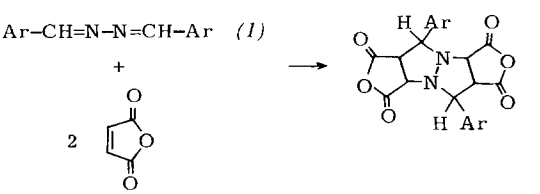
expansion, and by ring contraction. Modifications of the resulting β-lactam considerably extend the scope of these syntheses; derivatized penicillins and cephalosporins are of considerable importance. [Synthetic Routes to β-Lactams. Chem. Soc. Rev. *5*, 181–202 (1976); 170 references]

[Rd 880 IE—F]

Structural chemistry within zeolite A is the theme of a survey by *K. Seff*. Zeolites are aluminosilicates having a relatively rigid anionic skeleton and crystallographically well defined channels and cavities in which are located exchangeable cations, and in some cases guest molecules such as water which can also be replaced. Zeolites act as catalysts, ion exchangers, and selective sorption agents. Accurate structural determinations on zeolite single crystals prepared in various ways and having different cations and guest molecules should help us to understand the mode of action of zeolites. [Structural Chemistry inside Zeolite A. Acc. Chem. Res. *9*, 121–128 (1976); 32 references]

[Rd 882 IE—L]

Reactions of azines and imines with dienophiles are discussed by *T. Wagner-Jauregg*. Aromatic aldehyde azines *(1)* undergo criss-cross addition with two equivalents of dienophile to give 1,5-diazabicyclo[3.3.0]octane derivatives. This singular mode of reaction of *(1)* is observed not only with typical dienophiles like maleic anhydride but also with cyanic acid, thiocyanic acid, or phenyl isocyanate. Hexafluoroacetone azine also adds two equivalents of electron-rich olefins, azomethinimines being detected as intermediates. Schiff bases of aromatic



aldehydes undergo 1,4-cycloaddition with acetylenic dienophiles to give partially hydrogenated pyridines, and with olefinic dienophiles to form spiro compounds.—The article also considers the numerous types of dienophile addition to heterocycles having C=N double bonds and to azines and Schiff bases of cyclic ketones. [Reaktionen von Azinen und Iminen (Azomethinen, Schiffschen Basen) mit Dienophilen. Synthesis *1976*, 349–373; 153 references]

[Rd 883 IE—M]

Reaktionstypen in der anorganischen Chemie (Reaction types in inorganic chemistry). By *I. Fitz*. Akademie-Verlag, Berlin 1975. 1st Edit., 465 pp., 98 figures, 105 tables, bound, DM 58.—

This book, which is concerned with the laws governing inorganic reactions in aqueous solution, is divided into nine sections. A general chapter about bonding and chemical reactivity is directly followed by an account of the principles of chemical reaction—then follow the most important types of reaction: complex reactions, redox reactions, and acid-base reactions. The work concludes with polymerization and depolymerization reactions, coupled reactions, and a survey of the common and distinguishing features of inorganic reaction types.

The first chapter mainly compares and contrasts the various kinds of chemical bonds, not always as clearly as desired. Terms such as bond lengths, ionic and atomic radii, force constants, bond energies, polarizability, electronegativity, and electron affinity have not been forgotten. It ends with a brief introduction to ligand field theory.

Before describing the three reaction types, the author attempts to clarify the principles of a chemical reaction by demonstrating the significant role of thermodynamics and kinetics in inorganic reactions in aqueous solution. Free energy and free enthalpy are just as important as, say, entropy in complex chemistry. Terms connected with kinetics such as activation energy, transition state, kinetic isotope effects, steric influence, and electronic effects are considered in detail. Predictions of the course and mechanism of a chemical reaction on the basis of thermodynamics and kinetics conclude this section.

In connection with complex reactions particular emphasis is placed upon thermodynamic aspects and ligand field theory. A separate section is devoted to stereochemistry and the stereochemical consequences of substitution reactions whose mechanisms are discussed with the aid of numerous examples.

Among the most important reaction types in organic chemistry are redox and acid-base systems. In both cases we are concerned with "particle-transfer reactions". An historical development of the concepts is given, and all relevant modern theories are mentioned. In such cases the present book replaces an analytical textbook for the treatment of redox equilibria and all kinds of pH calculations are discussed in the same great detail as the double logarithmic Hägg diagrams of corresponding acid-base pairs.

The work supplements available inorganic and analytical textbooks for undergraduates, even though the subject matter is sometimes of a more advanced nature. Clear tabulations of data are abundant. It is only regrettable that a number of factual and printing errors have crept into the book. Thus not all alkali halides have the NaCl structure, as claimed in Table 9. Table 16 contains misleading printing errors in the hybridizations and bond angles; the examples of Table 17 would have been better in Table 16. A better choice of examples would also have been desirable. For this reason the book can only be recommended with reservation.

Ekkehard Lindner [NB 328 IE]

Lehrbuch der Elektrochemie (Textbook of Electrochemistry). By *J. Koryta, J. Dvořák,* and *V. Boháčková*. Translated by *Helga Bažantová*. Springer-Verlag, Vienna—New York 1975. 1st Edit., xv, 348 pp., 108 figures, bound, 145.—.

The decision to market a translation of the Czech work "Textbook of electrochemistry" probably represents something of a gamble, particularly since the opportunities for developing a completely new concept deviating from the usual presentation and didactic approach are rather limited. Although the treatment of individual topics in this book resembles that in other textbooks, a certain degree of originality is to be seen in the subdivision of the material.

Our attention is first directed to equilibria in electrolytes, a brief introduction containing definitions of equilibrium constants and activities and activity coefficients being followed immediately by the Debye-Hückel law and its extension, as well as methods for determining the activity coefficients of electrolytes. There follow the theory of weak electrolytes and a consideration of the pH value, paying attention to varying definitions and acidity functions. The chapter closes with an account of ampholytes and polyelectrolytes.

The second chapter is concerned with the transport processes so important for practical electrolysis and electrochemical methods of analysis. Not only diffusion and migration, but also convective diffusion, which is frequently neglected in other books, are all considered.

The third chapter discusses equilibria in heterogeneous electrochemical systems, *i.e.* equilibrium electrode potentials or equilibrium cell potentials. The electrochemical double layer is also described.

A brief treatment of membrane electrochemistry follows in the fourth chapter, which closes with a very short account of the electrochemistry of biological membranes. The final chapter is devoted to electrode kinetics.

The book is supplemented by a mathematical appendix, in which the applications of Laplace transformation to the solution of the diffusion problems of Chapter 2 is presented.

On 320 pages the book deals with all the important fundamental aspects of electrochemistry in a correct, competent, and lively manner. Concerning the didactic concept, however, it should be mentioned that in the chapter on electrode kinetics the reader often misses the right figure at the right place, and that some of the figures do more to disguise the situation than elucidate it (Fig. 3.11a, 3.19, 5.2, 5.3).

Unfortunately the translator's German leaves much to be desired, containing numerous Anglicisms, Gallicisms, and old-fashioned expressions. These weaknesses, however, could easily be remedied in a second edition.

Hartmut Wendt [NB 329 IE]

Röntgenbeugung an Kristallen (X-Ray Diffraction by Crystals). By *K. H. Jost*. Akademie-Verlag, Berlin 1975. 1st edit., xii, 404 pp., 332 figs., 18 tables, bound, *ca.* DM 98.—.

Contrary to what might be assumed from the title, this book does not deal with the method of crystal structure determination. Instead, the origin of X-ray diffraction diagrams and their recording and evaluation are described.

After two introductory chapters on the excitation of X-rays and the fundamental concepts of crystallography, the production of diffraction diagrams is discussed with particularly detailed treatment of the influence of disorders, thermal motion of atoms, and superstructures. The procedures now customary for recording the diffraction patterns and for measuring intensities are then presented, and the newer types of apparatus such as the Gandolfi camera and the Kappa four-circle diffractometer are also mentioned. A relatively large amount of space is taken up by a description of the methods of evaluation in comparison with that devoted to the determination of unit cell dimensions, symmetry and intensity.

The last chapter deals with powder methods and their application. Noteworthy is that topics such as the investigation

of texture, indexing according to ITO for any desired symmetry, and the investigations of pressure and temperature variations are also discussed.

With its detailed and clear presentation of themes, which are seldom treated elsewhere, this book fills a gap and provides a valuable supplement to books previously available on crystal-structure determination. In spite of the rather high price it can thus be strongly recommended to all concerned with X-ray diffraction.

Joachim Strähle [NB 330 IE]

Zum Ablauf ionischer Polymerisationsreaktionen (The course of Ionic Polymerizations). By *G. Heublein*. Akademie-Verlag, Berlin 1975. 1st edit., viii, 316 pp., numerous figs. and tables, bound, *ca.* DM 58.—.

In comparison with the industrially much more important field of radical polyreactions there are considerably fewer proven results on ionic polymerizations. Thus, it is only in recent years that many of the "classical" concepts of cationic polyreactions have had to be revised. A critical presentation of the present state of our knowledge of ionic polyreactions is thus a difficult but undoubtedly highly valuable exercise.

Following a brief comparison of ionic and radical polymerizations and a general outline of the course of ionic polymerizations, the book treats first cationically and then anionically initiated polyreactions; a subsequent chapter is devoted to ionic copolymerizations. In a section contributed by *P. Hallpap* the current possibilities for quantifying description of ionic polymerizations are collected together with their quantum-chemical treatment.

A field as wide as this cannot be described in all its parts in equal detail; one misses, *e.g.* the recent investigations by *P. H. Plesch*'s school on cocatalyst-free cationic initiation of polymerization with aluminum trichloride and the pseudocationic polymerizations by ester formation. Objections in principle must be noted concerning some of the concepts used; the phrase "Mischpolymerisation" (mixed polymerization) should be finally banned from scientific literature according to IUPAC rules. To describe the growth step of polymerizations as the "Polyadditionsschritt" (polyaddition step) (*e.g.* p. 16), is at least an error of judgement, since in German it can easily lead to confusion with other polyadditions occurring according to totally different mechanisms.

These minor details do not, however, detract from the book's value as an easily readable summary for a currently important area of macromolecular chemistry, particularly as the more than 600 literature references make it possible to delve deeper into the subject. A more serious deficiency—and one that must certainly be corrected in a new edition—is the absence of a subject index, particularly as the contents list is only crudely sectionalized.

Dietrich Braun [NB 331 IE]

IR-Spektroskopie—Eine Einführung. (Taschentext 43/44) (IR Spectroscopy—An Introduction. Pocket book 43/44). By *H. Günzler* and *H. Böck*. Verlag Chemie/Physik Verlag, Weinheim 1975. 1st edit., xv, 363 pp., 152 figs., 50 tables, paperback, DM 38.—.

The main emphasis of this book is laid on the description of group frequencies of organic compounds, which are discussed very expertly with the aid of many original spectra and tables. Inorganic compounds are mentioned in only one sentence. Details of the apparatus, its maintenance, and of the preparation of samples are discussed at length; this part is of real practical value even for the experienced user, and treatment of special techniques takes up much space.

Theoretical principles up to the rotational vibration spectra of an anharmonic oscillator are treated in only 30 pages. Without giving any derivation the authors cite the Schrödinger equation as a kind of magic formula from which everything else can follow; here there are formulations that run from the unfortunate through the inexact to the false, and other chapters too are not free from them.

Because of the weaknesses in its treatment of the theoretical principles and its concentration on applications in organic chemistry, this book is certainly no general introduction to IR spectroscopy. The limitation to organic compounds should have been stated in the title.

Gerhard Lehmann [NB 332 IE]

Fortschritte der Massenspektrometrie. Progress in Mass Spectrometry. Edited by *H. Budzikiewicz*. Vol. 3. Alkaloide, ausser Indol-Triterpen-, und Steroidalkaloide. By *M. Hesse* and *H. P. Bernhard*. Verlag Chemie, GmbH, Weinheim 1975. 1st edit., xvii, 372 pp., 112 figs., 83 tables, bound, DM 148.—.

In order to take into account the complexity and structural variety of this group of natural products the authors confine themselves in this book in the Progress series[*] to the nitrogen compounds that are not classifiable as indole, triterpene, steroid, or ergot alkaloids. The classification principle for the remaining compounds—structurally considered still imposing in number—is based on the practicable but not always relevant assumption that in alkaloids the decompositions induced by electron impact generally start from ionized nitrogen. In consequence, therefore, the "nitrogen" structural element is set up as the centerpoint, while the traditional classification based on skeletal or chromophore type and on biogenetic relationships serve as secondary classification characteristics.

The presentation of the immense volume of material succeeds by skilful choice and combination of line spectra, principal routes of decomposition, conclusions by analogy (allowed and forbidden), critical commentaries on spectral interpretation, and a comprehensive literature search (1082 references distributed over seven main chapters that in turn are subdivided into 125 fields). The authors have succeeded very well indeed in directing the reader rapidly and clearly (often with use of structural formulas) to the data relevant to analytical use by means of precise formulation and designation of key fragments. Mechanistic aspects are, in general, considered and used for spectral interpretation only insofar as they have been proved by experiment.

In spite of the extensive data material involved (an index, arranged by molecular weight and names of 1260 compounds, as well as a comprehensive subject index allow rapid orientation), this book will not only be valuable to the typical alkaloid chemist but will also prove to be a (provocative) source for mechanistic studies, as repeatedly indicated by the authors' views and limits. How helpful and important is well-based knowledge of the decomposition principles for a correct interpretation of the mass spectra of alkaloids is shown impressively by Chapter 6 (putrescine, spermidine, and spermine alkaloids). On the basis of studies of model compounds, carried out by the Zurich group, it is demonstrated, *inter alia*, that the apparent complexity of the mass spectra of these alkaloids is due to the simple interaction of nonbonded centers (*e.g.* specific, reciprocal H-transfers or electron-impact-induced S_Ni reactions).

The book constitutes an important addition to the standard works already available for chemists concerned with the analytical side of alkaloid chemistry.

Helmut Schwarz [NB 333 IE]

[*] Cf. Angew. Chem. Int. Ed. Engl. *15*, 58 (1976).

Chemische Reaktionstechnik (Chemical Reaction Engineering). By *K. Dialer* and *A. Löwe*. Carl Hanser Verlag, Munich–Vienna 1975, 1st edit., 108 pp., 44 figs., 8 tables, board, DM 22.—.

This monograph is intended as an introduction to the field, aimed in particular at chemists and process engineers. It should serve chemists as a supplement to the usual sectors of chemistry and as an insight into the application of chemical and physicochemical principles to the planning and design of industrial installations, especially reactors. The relationships between unit operations and processes for conversion of materials are indicated for the benefit of chemical engineers.

The authors' aim has been to offer "a brief systematic introduction to the principles of reaction engineering, and especially as a concise revision of examination material".

The basic principles of reaction engineering are first explained, starting from a good introduction into the importance and systematics of the field, and are followed by the essentials of homogeneous and heterogeneous reactions. Simple methods of designing chemical reactors are first discussed, followed by the complex relationships between ideal model presentations and real conditions. The following chapters treat the possibility of performing the process with different aims in view, *e.g.* conversion, yield, selectivity, *etc.* Finally, there are questions of application, such as acquisition of data, scaling up, and optimization. The book presents a successful selection of the most important themes from the broad field of chemical reaction engineering, and does so meaningfully. Particularly praiseworthy is the excellent collection of references that extend to very recent times and make it possible to handle problems of industrial reactions in a manner corresponding to the current state of the art. Because of the brief and concentrated presentation, however, only those who already have some previous knowledge of reaction kinetics and transport processes will get full value out of the monograph.

K. H. Simmrock [NB 336 IE]

Advances in Carbohydrate Chemistry and Biochemistry, Vol. 32. Edited by *R. S. Tipson* and *D. Horton*. Academic Press, New York 1976. x, 439 pp., bound, $ 42.00.

Ionic Polymerization. Unsolved Problems. By *J. Furukawa* and *O. Vogl*. Marcel Dekker, New York 1976. ix, 450 pp., bound, SFr. 150.00.—1st Japan-US Seminar on Polymer Synthesis.

Enzy.-katalysierte Reaktionen. By *C. J. Gray*. Gustav Fischer Verlag, Stuttgart 1976. 383 pp., paper, DM 39.50.

Poly(ethylene oxide). By *F. E. Bailey, Jr.* and *J. V. Koleske*. Academic Press, New York 1976. ix, 173 pp., bound, $ 13.00, or £ 7.95.

Fluorocarbon and Related Chemistry, Vol. 3. Senior Reporters: *R. E. Banks* and *M. G. Barlow*. The Chemical Society, London 1976. ix, 491 pp., bound, £ 35.00.—A volume of the series "Specialist Periodical Reports".

Übungsaufgaben zur Mathematik für Chemiker. By *J. Fuhrmann* and *H. G. Zachmann*. Volume 45 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1976. vi, 280 pp., paper, DM 24.00.

Applied Spectroscopy Reviews, Vol. 10. Edited by *E. G. Brame, Jr.* Marcel Dekker, New York 1976. xv, 305 pp., bound, $ 32.50.

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RKW-Handbuch Forschung, Entwicklung, Konstruktion (F+E). By *H. Moll* and *H. J. Warnecke*. Erich Schmidt Verlag, Berlin 1976. Basic instalment 278 pp., Loose-leaf file DM 9.80.

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Polar Effects in Organic Reactions

By Cyril A. Grob[*]

Attempts to gauge the effect of polar substituents on organic reaction rates by means of "inductive substituent constants" are based on the assumption that these effects are independent of the type of reaction observed. The measured rate constants of nucleophilic substitution reactions show, however, that this assumption is only partly justified even for saturated molecules. It is invalid if the substituent and the reaction center are an electron donor and an electron acceptor, respectively, which are hyperconjugated by way of σ-bonds. In extreme cases the resulting polarization can lead to heterolytic fragmentation.

1. Introduction

The common description of organic compounds by symbols such as ROH, RCHO, or RCOOH implies that chemical changes occur at the functional groups, in the above cases at the hydroxyl, formyl, or carboxyl group, respectively, while the rest of the molecule is left unaffected. In view of the large number of organic compounds and their variety it would not be possible to describe their reactions without this simplification. However, the study of structure-reactivity relationships and physical properties of organic molecules soon shows that the functional group is affected by the group R in at least three different ways, *i.e.* by polar, conjugative, or steric effects[1].

Steric effects are most easily visualized because they can be described simply in terms of space-filling and the impenetrability of atoms. Conjugative effects such as occur in unsaturated, conjugated molecules, are harder to interpret. Intermediate are the polar effects of monopolar and dipolar substituents that are not conjugated with the reaction center but influence it electrostatically. These three effects are rarely observed in isolation, but their conceptual differentiation is of great value, especially for didactic purposes.

This article is concerned with the polar effects of substituents in saturated compounds, first with new attempts to assess them quantitatively by assigning them so-called inductive substituent constants. For this purpose the model with which the transmission of the substituent effect is described, *i.e.* the field model or the inductive model[1], is irrelevant[*]. Ideally such constants should gauge the influence of the substituent on the reaction center correctly and independently of the nature of the reaction. The third and fourth sections of this review are therefore devoted to the question whether the new constants are able to correctly correlate polar substituent effects in simple reactions.

2. Determination of Inductive Substituent Constants

The dissociation constants K_a (or the pK_a values) of carboxylic acids [reaction (a)] have long been used to detect and to measure polar effects quantitatively[3].

$$RCH_2COOH + H_2O \overset{K_a}{\rightleftharpoons} RCH_2COO^{\ominus} + H_3O^{\oplus} \qquad (a)$$

On this basis chloroacetic acid (R = Cl) is *ca.* 80 times stronger than acetic acid, and trimethylammonioacetic acid [$R = (CH_3)_3N^+$] [more precisely, the carboxymethyl(trimethyl)ammonium cation] is *ca.* 100 times stronger. The examples illustrate the powerful effect of the C—Cl dipole and particularly of the positive monopole on the equilibrium. Nor have attempts been lacking to apply the pK_a values of substituted acetic acids to the definition of inductive substituent constants, *e.g.* by *Charton*'s σ_I constants[4], which are proportional to the pK_a values.

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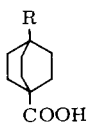
[*] New findings, however, clearly indicate the superiority of the former (electrostatic) model [2].

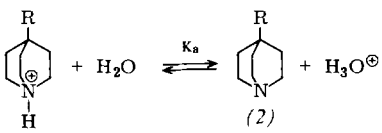
However, the substituent constants derived in this way have only limited validity, because the dissociation constants and even the relative strengths of carboxylic acids are strongly temperature-dependent[5], the reason being that the entropy term $T\Delta S^0$ contributes more strongly to the free dissociation enthalpy ΔG^0 than does the enthalpy term ΔH^0[*] as a result of the large increase in solvation when a neutral acid is ionized according to reaction (a). Furthermore, bulky α-substituents hinder solvation of the anion, so that steric effects may be superimposed on the polar effects[6].

Another frequently used method for the quantitative evaluation of polar effects is one due to *Taft*[7]. This method is based on measurements of the differences between the rates of acid and alkaline hydrolysis of acetic esters. The basic assumption underlying this method, *i.e.* that steric effects are thereby eliminated, has recently been questioned[6, 8]. Nevertheless, substituent constants σ_I or σ^* ($\sigma_I = 0.45\,\sigma^*$[7]) derived in this way have often been used with success in studies of structure-reactivity relationships.



(1)

The pK_a values of rigid bicyclic acids, such as the 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids *(1)* studied by *Roberts*, are largely free from steric influences[9]. In these acids the substituent R is at a considerable distance from the reaction center and the measurable polar effect is consequently rather weak, a disadvantage in addition to the temperature dependence of the pK_a values of carboxylic acids mentioned above.



(b)

(2)

These disadvantages do not apply to the 4-substituted quinuclidines *(2)* investigated by us[10] and by others[11]. In these highly symmetrical compounds the bond to the 4-substituent lies on the molecular axis and is relatively close to the reaction center (*ca.* 2.5 Å) without sterically hindering solvation. In addition, the polar effect is transmitted through a region of low effective dielectric constant, and should thus act strongly on the pK_a values and be largely independent of the solvent. What is of particular importance is that in reaction (b) two cations are in equilibrium with one another. Therefore solvation and thus the contribution of the temperature-dependent entropy term to the free energy of the reaction is less important than it is for the carboxylic acid models. These advantages are somewhat offset by the difficulties encountered in synthesizing the compounds *(2)*[10] and which have presented an obstacle to systematic studies. In spite of this, the pK_a values of some forty representatives in water have been measured[12].

The results obtained so far appear to fulfil these expectations, in that polar effects are particularly strongly transmitted. Thus, the difference between the strongest base, 4-*tert*-butylquinuclidine, and the weakest, 4-nitroquinuclidine, is 3.63 pK_a units. This difference is greater than that for the corresponding substituted acetic acids, where it is only 3.08 units although in the latter case the substituents are separated from the dissociating proton by one less σ-bond.

The pK_a values of the quinuclidines studied so far at several temperatures show that the enthalpy term ΔH^0 is the main contributor to the free enthalpy of dissociation ΔG^0 and that the entropy term $T\Delta S^0$ is much less important than in reaction (a)[12]. Moreover, in the cases so far studied by us the influence of the substituents has proved to be almost independent of the dielectric constant (DC) of the solvent. For example, the decrease in the pK_a value of quinuclidine due to the 4-acetyl group was *ca.* 13 % in water ($DC = 78$), 80 % methylcellosolve ($DC = 33$), 50 % ethanol ($DC = 49$), and in 80 % ethanol ($DC = 35$). The decrease in pK_a due to the 4-cyano group was *ca.* 26 % in all four solvents. The polar effect is therefore transmitted almost entirely within the molecule.

On the basis of the pK_a values of quinuclidine (pK_a^H) and its 4-derivatives (pK_a^R) in water at 25 °C the new inductive substitution constants σ_I^q can be defined as:

$$pK_a^H - pK_a^R = \rho\,\sigma_I^q$$

where ρ is the reaction constant, which is arbitrarily chosen as unity. The letter q in the symbol σ_I^q indicates that quinuclidines act as models. Table 1 lists some of the substituent constants determined in this way (an exhaustive list is given in [12]).

Table 1. Inductive substituent constants σ_I^q derived from pK_a values of 4-R-substituted quinuclidines *(2)*.

R	σ_I^q	R	σ_I^q
H	0	$COCH_3$	1.69
CH_3	0.11	$CONH_2$	1.82
C_2H_5	0.03	CN	3.04
i-C_3H_7	−0.08	NH_2	0.98
t-C_4H_9	−0.15	$N(CH_3)_2$	0.97
CH_2OH	0.66	NO_2	3.48
CH_2NH_2	0.52	OH	1.74
CH_2Br	1.07	OCH_3	1.81
$C(CH_3)=CH_2$	0.60	SCH_3	1.66
$C\equiv CH$	1.64	F	2.57
C_6H_5	0.94	Cl	2.51
COO^-	0.58	Br	2.65
$COOC_2H_5$	1.70	I	2.34

It would lie beyond the scope of this article to discuss each individual constant here, but some important findings deserve special mention. The basicities of the 4-alkylquinuclidines, namely the methyl, ethyl, isopropyl and *tert*-butyl derivatives, whose polar effects have now been reliably determined by pK_a measurements for the first time, increase in the expected order[1]. The differences are small, as also in the case of the 3-alkylquinuclidines *(3)*[10c], but they are nonetheless significant. Thus the usual order for the inductive effects of the alkyl groups is found[1], except for the position of hydrogen within the series. In fact, the methyl group proves to be somewhat base-weakening, the ethyl group almost equivalent to hydrogen, thus confirming more recent observations[13]. However, this order applies only when these groups are bonded to a saturated, *i.e.* sp^3-hybridized, carbon atom, for on unsaturated sp^2-hybridized carbon the methyl group is distinctly base-strengthening. This follows from the pK_a values for

[*] For example, in the case of acetic acid $T\Delta S^0$ and ΔH^0 are respectively −6.57 and −0.137 kcal/mol [5].

dehydroquinuclidine *(4a)* (9.88) and for its 3-methyl derivative *(4b)* (10.11)[14].

(3)

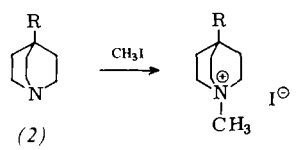
(4a), R = H
(4b), R = CH_3

As expected, the alkenyl, alkynyl, and aryl groups are electron-attracting as compared with alkyl groups. This applies particularly to groups containing heteroatoms, the most effective ones being the halogens, the cyano, and the nitro group.

If the σ_I^q values and the σ_I constants of *Taft* and *Charton* mentioned above were equivalent measures of polar substituent effects, then there should be a linear relationship between them. They do indeed correlate to a certain extent, but not particularly well[12] (*i.e.* with correlation coefficients of 0.906 and 0.949, respectively). The deviations are probably due to the different models (quinuclidines, acetic esters, acetic acids) and reactions (pK_a values and rate constants), used in the determination of the substituent constants—an indication of the problems in defining generally valid polar substituent constants.

3. Substituent Effects in a Bimolecular Nucleophilic Substitution

How then do the new σ_I^q values stand the test of correlating substituent effects in simple nucleophilic substitution reactions? As a first example let us consider the quaternization of 4-substituted quinuclidines *(2)* with methyl iodide in methanol, a bimolecular (S_N2) nucleophilic substitution [reaction (c)]. This Menshutkin reaction is very similar to the standard reaction (b) insofar as here too the nitrogen adopts a positive charge; however, in contrast to protonation, reaction (c) is irreversible.



(2) (c)

Measurement of the second-order rate constant for thirty 4-substituted quinuclidines[15] shows that quaternization responds less strongly to polar substituent effects than does the protonation reaction (b). For example, 4-nitroquinuclidine, which is less basic than quinuclidine by 3.48 pK_a units, reacts 6.7 times slower than the latter, indicating that less positive charge has developed in the transition state of the reaction. Furthermore, if the logarithms of the second-order rate constants ($\log k$) are plotted against the corresponding σ_I^q values, there is considerable scattering around the regression line (Fig. 1, correlation coefficient 0.975).

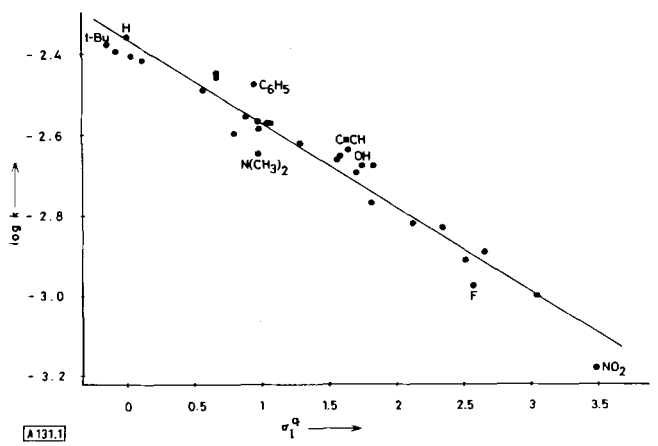


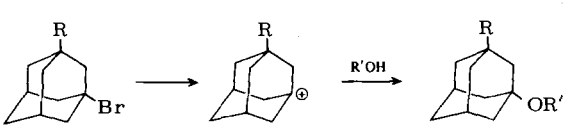
Fig. 1. Relationship between $\log k$ for the quaternization of 4-substituted quinuclidines *(2)* by methyl iodide [reaction (c)] and the inductive substituent constants σ_I^q. Only some of the substituents are considered in the Figure.

Only a small part of this scattering can be caused by solvent effects, *e.g.* hydrogen bonding between methanol and the quinuclidine nitrogen[16], as shown by analysis of the deviations and by experiments in acetonitrile. The scattering should rather be ascribed to the fact that in this case substituent effects on a reversible reaction (pK_a) are compared with those on an irreversible reaction ($\log k$). Thus, it is assumed that the substituents influence equilibrium constants and rate constants in the same way and that the free reaction enthalpies and the free activation enthalpies are strictly proportional to one another. This assumption upon which free-energy relationships, such as the Hammett equation[17], are based has certainly only limited validity, a fact that is usually overlooked.

The slope of the regression line in Figure 1 gives a reaction constant ρ of -0.21. For the reversible protonation of 4-substituted quinuclidines *(2)* [reaction (b)] the value of ρ was arbitrarily set at 1. The above negative value of ρ thus confirms that quaternization [reaction (c)] responds less strongly to polar substituent effects, and moreover, it does so in the opposite direction.

4. Substituent Effects in a Solvolytic Reaction

Polar substituents should have a more marked effect on the formation of carbenium ions than on the production of ammonium ions. The former event occurs in the solvolysis of 1-substituted 3-bromoadamantanes *(5)* in 80% ethanol, in that ionization to the adamantanyl cations *(6)* is involved in the rate-determining step [reaction (d)]. In a rapid subsequent step these cations are converted into adamantanols *(7a)* and their ethyl ethers *(7b)*.



(5) *(6)* *(7a)*, R' = H
(7b), R' = C_2H_5 (d)

The question is whether the ionization of *(5)* is influenced by the substituent R in the same way as the reversible protonation of the corresponding quinuclidines *(2)*. If the polar substituent effects were generally valid, there should be a linear relationship between the σ_I^q values and the logarithms of the rate constants ($\log k$), since the latter are proportional to the free activation enthalpies of ionization.

Recently we have prepared and investigated some of those 1-substituted 3-bromoadamantanes *(5)* for which the σ_I^q values of the substituents are known[18]. The first-order rate constants (k) and the relative k values (relative to R = H) are listed in Table 2 together with the corresponding σ_I^q values[12]. (Some of these rate constants had been determined

previously[13c, 13d, 13f].) In Figure 2 the logarithms of the rate constants (log$k$) are plotted against the σ_I^q values.

Table 2. Absolute and relative first-order rate constants of 1-R-substituted 3-bromoadamantanes *(5)* in 80 vol-% ethanol at 70.0°C, inductive substituent constants σ_I^q (see Table 1), and acceleration of the solvolysis of *(5)* derived from the regression line in Figure 2.

	R	$k \times 10^5$ [s^{-1}]	k_{rel}	σ_I^q	Acceleration
(a)	H	7.16	1	0	
(b)	CH_3	5.31	0.742	0.11	
(c)	C_2H_5	7.28	1.02	0.03	
(d)	i-C_3H_7	10.9	1.52	−0.08	
(e)	t-C_4H_9	16.6	2.32	−0.15	
(f)	CH_2Br	0.35	0.049	1.07	
(g)	COOH	0.0748	0.0104	1.7	
(h)	Br	0.0084	0.0012	2.65	
(i)	CH_2OH	4.26	0.595	0.66	3.2
(j)	CH_2NH_2	4.89	0.682	0.52	2.6
(k)	$CONH_2$	0.158	0.0221	1.82	2.5
(l)	COO^-	15.67	2.19	0.58	9.7
(m)	$C(CH_3)=CH_2$	2.60	0.363	0.60	1.7
(n)	C_6H_5	1.55	0.216	0.94	2.5
(o)	SCH_3	0.294	0.041	1.66	3.0
(p)	OCH_3	0.975	0.136	1.81	15
(q)	OH	3.40	0.475	1.74	44
(r)	NH_2	267	37.3	0.98	4.7×10^2
(s)	$N(CH_3)_2$	8500	1187	0.97	1.5×10^4
(t)	O^-	*ca.* 500000	*ca.* 70000		

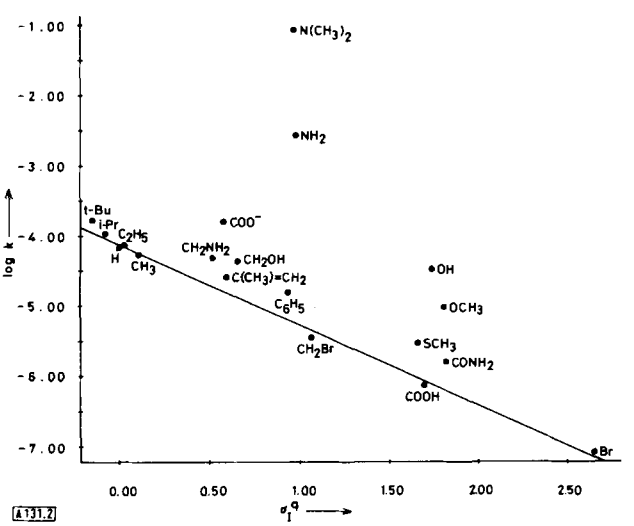
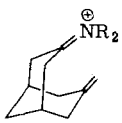


Fig. 2. Relationship between log$k$ for solvolysis of 1-substituted 3-bromoadamantanes *(5)* in 80 vol-% ethanol [reaction (d)] and their inductive substituent constants σ_I^q.

The substituents R in compounds *(5a)* to *(5t)* (Table 2) can be divided into three groups on the basis of the products formed in the reaction and the distribution of the points in Figure 2. The first group comprises the derivatives *(5a)* to *(5h)*; these react exclusively by substitution to yield *(7a)* and *(7b)*, and their log$k$ values correlate very well with the σ_I^q (correlation coefficient 0.998) with the exception of the *tert*-butyl derivative *(5e)*. The compound *(5e)* reacts 1.5 times as fast as would be expected on the basis of the regression line in Figure 2, and borders on the second group which comprises compounds *(5i)* to *(5p)*. This second group also reacts by substitution, but the correlation between log$k$ and σ_I^q can no longer be recognized, since the compounds react 1.7 to 15 times faster than predicted by the respective inductive substituent constants. The last column of Table 2 shows the accelerations based on the regression line in Figure 2[19].

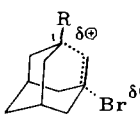
Finally, a third group can be recognized, comprising the derivatives *(5q)* to *(5t)*. Ionization of these compounds is accelerated still more strongly and, in contrast to the previous two groups, heterolytic fragmentation also occurs (for definition of this reaction type cf.[20]). Thus, 3-bromoadamantanol *(5q)* and the corresponding alkoxide *(5t)* formed in the presence of sodium hydroxide yield on solvolysis the unsaturated ketone *(8)* in yields of 70 and 100% respectively. The amines *(5r)* and *(5s)* fragment quantitatively to the immonium ions *(9a)* and *(9b)*, respectively, as previously observed[21].

(8)



(9a), R = H
(9b), R = CH_3

The calculated acceleration of the alcohol *(5q)* is 44, and that of its conjugate base *(5t)* can be estimated to be greater than 10^5[*]. For the amines *(5r)* and *(5s)* the acceleration of ionization due to the amino groups amounts to 4.7×10^2 and 1.5×10^4, respectively. There can therefore be no doubt that these four compounds fragment by the synchronous or concerted mechanism[**][23]. Their ionization is thus accompanied by fission of the C(1)—C(2) σ-bond and assisted by the frangomeric effect of the 1-substituent, as expressed in the representation *(10)* of the transition state[***].



(10)

Whereas the reactivity of the derivatives *(5q)* to *(5t)* is determined by the frangomeric effect of the substituents, it depends only on the polar effect of the substituents in compounds *(5b)* to *(5h)*, as shown by the good correlation between log$k$ and the corresponding σ_I^q values. The reaction constant ρ of -1.14 calculated from the slope of the regression line in Figure 2 shows that ionization of *(5b)* to *(5h)* responds only slightly more to the respective substituents than do the pK_a values of the 4-substituted quinuclidines *(2)* (by definition, $\rho = 1$); furthermore, the sign of ρ is reversed, *i.e.* ionization is retarded by electron-attracting substituents.

It is difficult to interpret the reactivity of compounds *(5i)* to *(5p)*, which also react by substitution but in some cases considerably faster than expected from the σ_I^q values of the 1-substituents.

Acceleration by the carboxylate *(5l)* and methoxy *(5p)* groups is particularly marked, amounting to factors of 10 and 15 respectively (Table 2). The smallest accelerations are caused by the methylvinyl and the *tert*-butyl group.

Since this additional effect only appears during the activation process, *i.e.* in the transition state of the reaction, it

[*] The pK_a and thus the σ_I^q value of the conjugate base of 4-hydroxyquinuclidine cannot be determined [12].

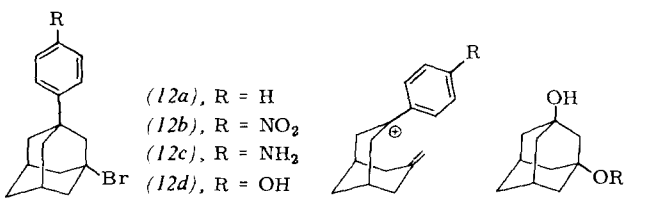
[**] We now a prefer the term "concerted" [22].

[***] The frangomeric effect is the acceleration of the ionization rate due to the concerted mechanism of fragmentation [23].

must depend on the polarizability of the substituents. An additional polarization occurring by the inductive[*] mechanism was called the inductomeric effect by *Ingold*[1,24]. This differentiation between the inductive effect operating in the ground state and the variable inductomeric effect appearing during the activation process is generally neglected due to a lack of experimental evidence. The findings discussed above appear, however, to justify this differentiation. Nevertheless, another less probable explanation for the higher reactivities of compounds *(5i)* to *(5p)* should also be mentioned.

(11) *(6)*

The solvolysis of compounds *(5q)* to *(5t)* shows that concerted fragmentation to give the ring-opened products *(8)* and *(9)* occurs when R is a strongly electron-donating group such as O^- or NR_2. (For further examples see [22].) The reactions occur with frangomeric acceleration, *i.e.* their rate is greatly increased in comparison with simple ionization to adamantanyl cations *(6)*. It is conceivable that compounds *(5i)* to *(5p)* also undergo concerted fragmentation, but that the cations of type *(11)* formed initially then rapidly recyclize to yield adamantanyl cations, which subsequently afford the substitution products *(7)* by the addition of water or ethanol. The products *(7)* would thus arise by a fragmentation and recombination process.



(12a), R = H
(12b), R = NO_2
(12c), R = NH_2
(12d), R = OH

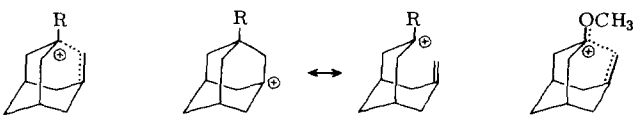
(12a) ≡ *(5n)* *(13)* *(14a)*, R = H
(14b), R = C_2H_5

The first objection to this hypothesis is that careful analysis of the reaction solutions has disclosed no trace of the products that would result from cations *(11)*; secondly, investigations of the reaction of 1-aryl-3-bromoadamantanes *(12a)* to *(12d)* in 80% ethanol which, like the reactions of *(5a)* to *(5h)*, leads exclusively to substitution products, shows that no intermediate conjugated, ring-opened cation *(13)* is formed. If the ionization led directly to such a cation then the logarithms of the rate constants should correlate with *Brown*'s substituent constants σ^+[25] and give rise to a strongly negative reaction constant ρ. However, the log*k* values correlate better with the normal *Hammett* σ_p constants with $\rho = -0.84$, as is to be expected for the formation of an unconjugated adamantanyl cation *(6)*.

Finally, mention should be made of the reaction of 3-bromo-1-adamantanol *(5q)*; this is a borderline case, since it leads to the fragmentation product *(8)* and the substitution products *(14a)* and *(14b)* in the ratio of 7:3. The substitution products could possibly be formed by fragmentation-recombination, *i.e.* by way of the unsaturated ketone *(8)* and its cyclization product, the cation *(6)*, R = OH, especially as in acid solutions *(8)* cyclizes to 1,3-adamantanediol *(14a)*. However, control experiments show that the unsaturated ketone *(8)* does not cyclize under the basic solvolysis conditions used for the alcohol *(5q)*, namely in the presence of 1 to 4 equivalents of triethylamine, so that this ketone cannot be a precursor of the substitution products. In this case, therefore, concerted fragmentation to the ketone *(8)* and ionization to 3-hydroxy-1-adamantanyl cation *(6)*, R = OH, are evidently competing.

The results of solvolyses of the 3-bromoadamantanes *(5)* show that the polar effects of substituents are not constant: on the contrary they adjust to the requirements of the particular reaction. We shall now consider how the substituents act upon the reaction center.

In the derivatives *(5b)* to *(5h)*, whose log*k* values correlate well with the σ_I^q values, the substituent effect can be transmitted by simple polarization of the σ-bonds, *i.e.* as in the 4-substituted quinuclidines *(2)*, the reversible protonation of which [reaction (b)] serves as a reference for the substituent effect. In the remaining derivatives *(5i)* to *(5t)* this polarization increases continuously until fission of the C(1)—C(2) bond, *i.e.* fragmentation, occurs. This point is reached at compound *(5q)*, *i.e.* when R = OH, because this group can stabilize the positive charge arising on C(1) in the transition state *(10)* by its +M effect.



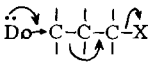
(15) *(6)* *(11)* *(16)*

Presumably delocalization of the electrons of the C(1)—C(2) bond also occurs in the transition state of ionization of the compounds *(5m)* to *(5p)*, thus leading to the mesomeric carbenium ion *(15)*. Description of this cation by the canonical forms *(6)* ↔ *(11)* makes it clear that the positive charge is distributed to C(3) as well as to C(1), where it can be stabilized by the substituents. The canonical forms also imply conjugation of a C—C bond with a cationic center, *i.e.* C—C *hyperconjugation*. An effect of this kind has been postulated in the past for S_N1 solvolyses but experimental evidence has so far been lacking[13c,13d].

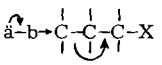
The distribution of positive charge over C(1) and C(3) is indicated also by the fact that the methoxy group in *(5p)* accelerates ionization five times as strongly as the methylthio group does in *(5o)* (Table 2) although oxygen exerts a greater electron-attracting effect than sulfur (as shown by the σ_I^q values). This surprising result indicates considerable delocalization of the free electron pair of the oxygen as shown in *(16)*, while delocalization is less pronounced in the thioether *(5o)* because of the weaker +M effect of sulfur[26]. The rate-enhancing effect of the methylvinyl *(5m)* and the phenyl group *(5n)* can be similarly explained, namely by delocalization of π-electrons. According to this view the rate-enhancing effect of the substituents in the derivatives *(5m)* to *(5p)* is due to the fact that an electron-donor Do is *hyperconjugated* to the reaction center, as formulated in *(17)*.

If this assumption is correct, heterolytic fragmentation occurs when hyperconjugation of a σ-bond merges with cleav-

[*] As opposed to a conjugative mechanism.



(17)



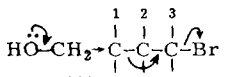
(18)

age, a process in which other than C—C bonds may be involved. These ideas correspond to the concept of "through bond coupling" recently derived by quantum-chemical (MO) calculations[27]. The calculations confirm also the stereoelectronic conditions for fragmentation as previously demonstrated experimentally[23] and which are satisfied in the adamantane derivatives *(5)*.

It is more difficult to interpret the rate-enhancing effect of the $HOCH_2$, H_2NCH_2, H_2NCO and ^-OOC groups in compounds *(5i)* to *(5l)*, which are unexpected on the basis of their σ_I^q values. A common feature is that they are potentially electrofugal groups a—b, *i.e.* they form a fragmentable system in combination with a central group c—d and a nucleofugal group X in accordance with reaction (e)[20].

$$a\text{–}b\text{–}c\text{–}d\text{–}X \longrightarrow a\text{–}b^{\oplus} + c{=}d + X^{\ominus} \qquad (e)$$

The four groups cited above thus act as electron-donors if coupled to a fragmentable system containing an acceptor, *i.e.* the nucleofuge. It then seems plausible that these same groups act as electron-donors if, in accordance with *(18)*, they are *hyperconjugated* to a cationic reaction center, as is the case with compounds *(5i)* to *(5l)*. Their role is not easy to describe with conventional symbols, especially since the $-I$ effect predominates, as shown by the k_{rel} values in Table 2. Nevertheless, the arrows in the partial formulas *(19)* to *(22)* do express the fact that these groups augment hyperconjugation of the C(1)—C(2) bond by increasing the electron density at C(1).



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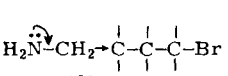

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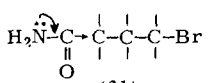

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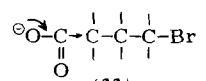
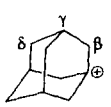


(22)

The resulting accelerations, by factors of 2.5 to 10, are relatively small and only partially compensate the inductive effect; but it is precisely small effects that are so difficult to detect and that often escape rational interpretation.

It remains to be mentioned that C—C hyperconjugation seems to appear even in the unsubstituted 1-adamantanyl cation *(23)*. This follows from its ^{1}H-NMR spectrum in the



(23)

non-nucleophilic medium SbF_5/SO_2[28] [chemical shifts (δ-values in ppm): 4.50 (H-β), 5.42 (H-γ), 2.67 (H-δ)]. In contrast to other tertiary carbenium ions, where the β-protons are most strongly deshielded, the signals of the γ-bridgehead protons appear at lowest field. This behavior is explicable if one assumes that in the unsubstituted cation also part of the positive charge is transferred to the γ-carbons as expressed in the canonical forms *(6)* ↔ *(11)*, R = H. This kind of stabilization was discussed previously by *Schleyer*[28,29] and by us[13c], but was regarded as unlikely because 1-bromo-3-methyladamantane *(5b)* reacts somewhat more slowly than 1-bromoadamantane *(5a)* itself (cf. Table 2). At that time it was believed that a 1-methyl group should favor C—C hyperconjugation in the cation *(15)*. However, now that it has been shown that a methyl group attached to an sp^3-hybridized carbon is electron-attracting relative to hydrogen (cf. Table 1), this objection is no longer valid. Moreover, the correlation between $\log k$ and σ_I^q in Figure 2 shows that more strongly electron-donating groups than alkyl groups are required to produce kinetically significant C—C hyperconjugation.

5. Conclusions

As shown in this review, the inductive substituent constants σ_I^q derived from pK_a values of 4-substituted quinuclidines *(2)* are of only limited use in predicting the polar effects of these substituents in other reactions of saturated molecules. Thus, in the quaternization of 4-substituted quinuclidines the rate constants show distinct deviations from the expected values. In the solvolysis of 1-substituted 3-bromoadamantanes *(5)* the correlation of the rate constants with σ_I^q is very good in some cases but non-existent in others. The deviations can be explained by the polarization of the substituents by the reaction center; this reaction-promoting effect is especially pronounced when strong electron-donors or potentially electrofugal groups are hyperconjugated with the reaction center.

Polar substituent effects thus depend on the nature of the reaction and are therefore variable, a view that has already become accepted for substituent effects in conjugated aromatic systems[30]. For this reason relatively narrow limits are imposed on all attempts to derive quantitative relationships between structure and reactivity.

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Kink-Block and Gauche-Block Structures of Bimolecular Films

By Gerhard Lagaly[*]

Layer silicates and some other layer compounds can take up organic compounds such as long-chain alkanols and alkylammonium ions with formation of ordered bimolecular films. This system enables new ideas to be developed concerning the structure of monomolecular and bimolecular films: the films form reversible kink-block and gauche-block structures. Conclusions can be derived about the structure of the lipid layers in membranes.

1. Introduction

The function of biological membranes[1, 2] is connected with bimolecular lipid layers which interact with proteins. *Robertson*'s model, and especially *Kreutz*'s model ("Basic structure of the biomembrane") give ideas of the association between lipid and protein layers[2–4] (Fig. 1).

The lipid layer can be regarded as a bimolecular lamellar array of long alkyl chains which act as supports for the proteins. However, this by no means exhausts their function. The similar, but not identical, chemical compositions of the lipid regions in many membranes[5, 6] and the significance of constituents of the lipid layers such as cholesterol, gangliosides, glycolipids and, especially, unsaturated compounds[7, 8] for the function of the membrane show that the lipid regions are active structural units of the membrane.

In order to understand the function of the lipid layers, systems with simplified chemical compositions containing monomolecular or bimolecular films have now been investigated for 50 years (Fig. 1). The films form several discrete phases; depending on the system, the phase transitions can be induced thermally[9–13], by variation of electrolyte concentrations[2, 14, 16–20], or by interaction with macromolecules[2, 21–23].

In spite of intensive investigations, little detailed information has so far been obtained about orientation and arrangement of the alkyl chains in the different phases. In most cases an order-disorder transformation from a crystalline to a liquid-like state through a kind of "chain melting" has been discussed[18, 24–29]. This interpretation attaches insufficient importance to the multiplicity of phase transitions in the region of the alkyl chain lamellas. What other possibilities, however, do alkyl chains have for forming different phases

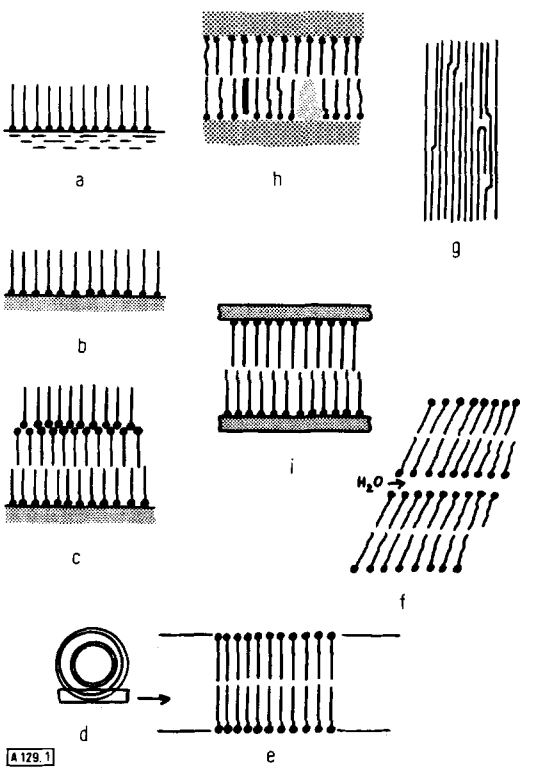

Fig. 1. Systems with mono- and bimolecular films of amphophilic molecules a) surface film on water or at water/oil interfaces [91]; b) monomolecular adsorption layers on solid surfaces; c) built-up films [92, 93]; d) liposomes [15]; e) black films [15, 91, 94]; f) lamellar structures of soaps, lipids, *etc.*, in water [9, 11, 16, 86, 95–97]; g) polymers; h) biological protein-lipid-protein membrane; i) bimolecular film in a layer crystal.

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in monomolecular or bimolecular films. Can simple structural types be found which are based as far as possible on a common principle?

We obtain additional information from a system that has been developed in solid-state chemistry and to which the most recent results from the physics of high polymers were applied: bimolecular films are formed between solid surfaces in layer crystals and are investigated by X-rays.

2. Preparation of Bimolecular Films in Layer Crystals

In the model system bimolecular films are built up between relatively rigid inorganic layers of layer compounds (Fig. 2). A wide range of layer compounds can be used: mica-type layer silicates[30,31], sodium silicates[32], niobates[33], uranates[34,35], vanadates[36,44], titanates[37,44], zirconium phosphates[38], graphitic acids[39], crystalline silicic **acids**[40], hydrated vanadium **oxides**[44], calcium salts of phosphoric acid **esters**[41], titanium disulfide[42].

The bimolecular films between the layers of mica-type layer silicates have been investigated in particular detail.

The starting materials are layer silicates such as vermiculite, beidellite, saponite, nontronite, hectorite, and the montmorillonites. The montmorillonites ("bentonites") are used on a large scale industrially as clay minerals. These minerals are built like mica and consist of silicate layers stacked on one another (Fig. 3)[45,46]. The layers are negatively charged, since in the tetrahedral layers Si^{4+} ions are replaced isomorphously by trivalent ions (Al^{3+} ions) and, in the octahedral layer Al^{3+} ions are replaced by divalent ions (especially Mg^{2+} but also Fe^{2+}) and Mg^{2+} ions by Li^{+} ions (hectorite). Cationic defects in the octahedral layers and possibly H^{+} defects ($V_{H^{\cdot}}$) on OH^{-} groups (OH^{-} replaced by O^{2-} and $V_{H^{\cdot}}$) contribute to the negative charge. In the micas the charge density is $\xi = 1.0$ eq/(Si, Al)$_4O_{10}$ unit; vermiculites have $\xi = 0.6$—0.8, beidellite $\xi = 0.4$—0.5, and montmorillonites $\xi = 0.2$—0.4[31,47]. To compensate the negative charges of the layer, cations (Ca^{2+}, Mg^{2+} or alkali-metal ions) are bound between the layers, and these can be exchanged by other cations.

To build up the films between the layers of the mica-type layer silicates, long-chain compounds must be introduced. It has been found that particularly uniform films with highly reproducible properties are formed when primary long-chain *n*-alkanols are used (Fig. 2). To avoid the influence of the small inorganic interlayer cations as point defects[43], the cations are replaced by primary long-chain *n*-alkylammonium ions, which then form the bimolecular film in combination with the alkanol molecules. (Experimentally, the inorganic interlayer cations are first replaced by the alkylammonium ions in aqueous solutions[30,31,47]. The alkylammonium deri-

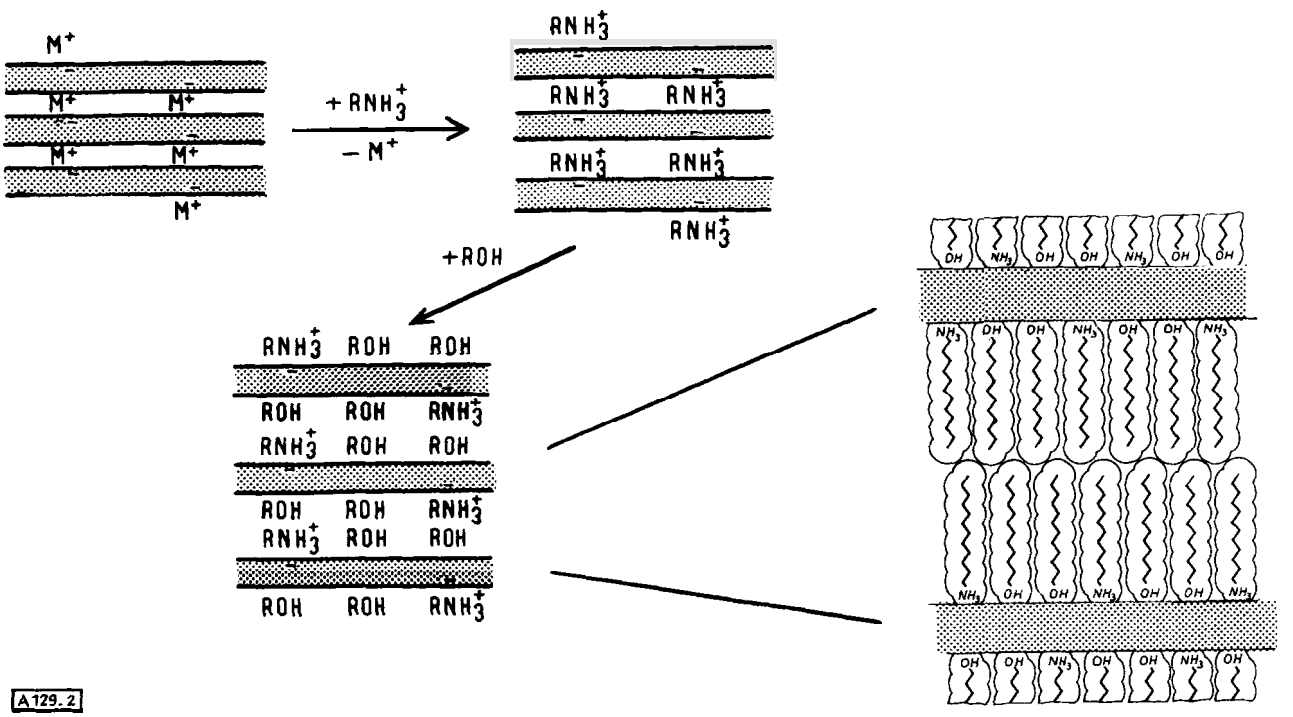

Fig. 2. Bimolecular films in an inorganic layer crystal formed by replacement of the interlayer metal cations by alkylammonium ions and incorporation of alkanol molecules ($R = C_nH_{2n+1}$, M^{+} = metal ion).

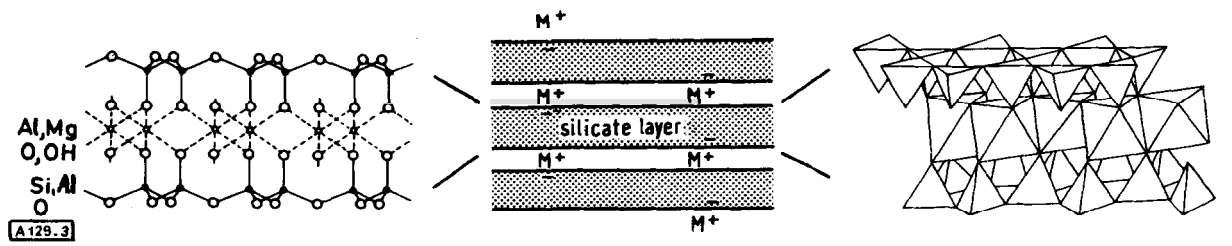

Fig. 3. Example of an inorganic layer compound suitable for the formation of bimolecular films in a layer crystal: mica-type layer silicates $M^{\xi}_{\xi}\{(Mg^{2+},Al^{3+},Fe^{2+},Fe^{3+})_{2\text{ to }3}(OH^{-},O^{2-},F^{-})_2(Si^{4+},Al^{3+},Fe^{3+})_4O_{10}\}^{\xi-}$.

vatives are then treated with the liquid alkanol, which is taken up between the layers within a few minutes[30, 31, 48].)

In films of alkyl chains of the same length or approximately the same length (maximum difference 6 C-atoms), two polar long-chain compounds, *i.e.* two alkyl chains, are bound per formula unit $(Si,Al)_4O_{10}$[31] because the polar end-groups of the long chain compounds are fixed in the pseudohexagonal holes in the tetrahedral sheets (Fig. 3, right). Small deviations from 2.0 chains per unit can occur[48].

Table 1. Examples of the average composition of bimolecular films in mica-type layer silicates. (Alkyl chains in the alkanol ROH and in the alkylammonium ion RNH_3^+ same or different, but the difference not too large [31]).

Layer crystal	Present per $(Si,Al)_4O_{10}$ unit: ROH	RNH_3^+	Ratio	Area/chain [Å]²
Muscovite	1.0	1.0	1.0	23.4
Vermiculite (South Africa)	1.3_3	0.67	2.0	24.5
Beidellite (No. III, Rhön)	1.5_7	0.43	3.65	23.3
Montmorillonite (Cyprus)	1.6_4	0.36	4.6	23.3
Montomorillonite (M 26, Wyoming)	1.7_2	0.28	6.1	23.3
Hectorite (H 1, California)	1.7_6	0.24	7.3	24.1

Table 1 gives the film compositions in the case of the layer silicates used most frequently. Since there are two alkyl chains in the bimolecular film per formula unit (=half the elementary cell), with an area of $a_0b_0/2 = 49$ Å² (vermiculites) and $a_0b_0/2 = 46.5$ Å² (montmorillonites and beidellite), the packing density of the chains is 24.5 and 23.2_5 Å²/chain (Table 1).

3. Phase Transitions in Bimolecular Films

3.1. X-Ray Results

The incorporation of alkylammonium ions and alkanol molecules between the silicate layers leads to the regular sequence: ... film—silicate layer—film—silicate layer—.... Since all films have the same thickness, in the X-ray diagram an integral series of (00l) interferences is observed up to high orders. From the d_{00l}-values the basal spacing $d_L = l d_{00l}$ is taken. The film thickness D can be estimated from the basal spacing d_L if the thickness of the silicate layer (9.5 Å) is deducted. Since the dimensions of the silicate sheets remain constant, any change in the film thickness is shown up in the basal spacing.

Characteristic changes take place with rising temperature (Fig. 4): both in films of alkyl chains of the same length and in films of alkyl chains of different lengths (*i.e.* alkanol molecules longer or shorter than the alkylammonium ions), the thickness of the film decreases in steps of 1—1.2 Å. A decrease of 1.1 Å is found particularly frequently[49]. The number of the steps increases with increasing chain length. In the case of chains of different lengths, the number depends on which of the two types of compounds has the longer chain.

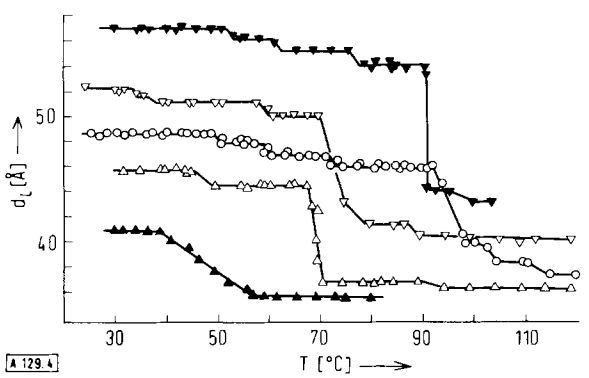

Fig. 4. Changes in the thickness of bimolecular films of alkylammonium ions and alkanol molecules between silicate layers (beidellite) with temperature. The following parameters are given: the basal spacing d_L; n_C = number of C atoms in the alkylammonium ion; n_A = number of C atoms in the alkanol; the ratio of alkylammonium ions to alkanol ≈ 0.43/1.57. △ $n_C = 10$, $n_A = 14$; ▲ $n_C = 14$, $n_A = 10$; ○ $n_C = 14$, $n_A = 14$; ▼ $n_C = 14$, $n_A = 18$; ▽ $n_C = 18$, $n_A = 14$.

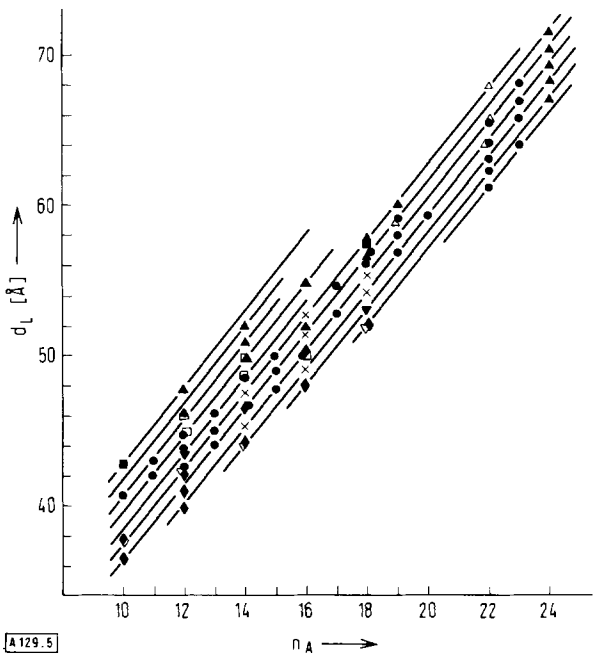

Fig. 5. Basal spacing d_L in the case of bimolecular films in *all-trans* block and kink-block structures (β-phases) between silicate layers: dependence on the number of C atoms in the alkanol (n_A). System as in Fig. 4 with ● $n_C = 10$, ▼, ▽ $n_C = 12$, ● $n_C = 14$, ■, □ $n_C = 16$, ▲, △ $n_C = 18$, × : Several coinciding values. *All-trans* denotes the extended saturated alkyl chain. For the term "kink-block structure", see Section 4.2.

Fig. 5 shows the basal spacings at the steps (see Fig. 4) for several combinations of chain lengths. They all form parallel straight lines separated by a distance of 1—1.2 Å, *i.e.* the observed basal spacings differ by 1—1.2 Å or a multiple thereof.

The temperature at which the film thickness decreases depends on the chain length and on the chain-length difference (Table 2). In general, the transition temperature rises somewhat with increasing length of the alkanol molecule (n_A). In the vertical series (increase in the length of the alkylammonium ions (n_C) at constant chain length of the alkanol) some irregularities occur; in most cases the transition temperatures also increase.

After the small steps of 1—1.2 Å, the basal spacing decreases drastically at higher temperatures by several Å. If the temperature rises further again small steps of 0.5—1 Å are observed. The maximum basal spacings of these high-temperature forms change somewhat less regularly with the chain length. Nevertheless, Fig. 6 shows that up to $n_A = 16$ they increase

Table 2. Transition temperatures within the series of kink-block phases [a] and for kink-block phases into gauche-block phases [a] (underlined figures); layer silicate: V: vermiculite (South Africa), B: beidellite; M: montmorillonite (Wyoming). n_C and n_A represent the numbers of C atoms in the alkylammonium ion and in the alkanol, respectively. The figures given are the temperatures at which the transition starts (decrease in film thickness).

n_C		$n_A=10$	$n_A=12$	$n_A=14$	$n_A=16$	$n_A=18$
10	B:	40; 70	30, 40; 70	30, 46; 68	30, 48; 68	—; 65
12	V:			46, 65; 73	50, 60; 70	30, 57; 70
	B:	30; 45	41, 58; 79	45, 65; 76	50, 65; 72	35, 55; 70
	M:		30, 45; 55	45; 60	35, 47; 60	30, 50; 60
14	B:	35; 40	35, 47; 68	47, 57, 70; 90	49, 58, 70; 90	35, 52, 62, 71; 89
	M:		40	45; 60	47, 55; 65	40, 55; 65
16	B:	30; 45	47; 60	40, ?; 71	57, 68; 94	60, 72; 90
	M:	30	45	45; 65	55, 65; 80	55, 75; 80
18	B:		25, 47; 67	37, 57; 70	35, 55, 73; 85	60, 73; 95
	M:		40	40, 50; 60	30, 50; 75	75

[a] These terms are explained in Sections 4.2 and 5.1.

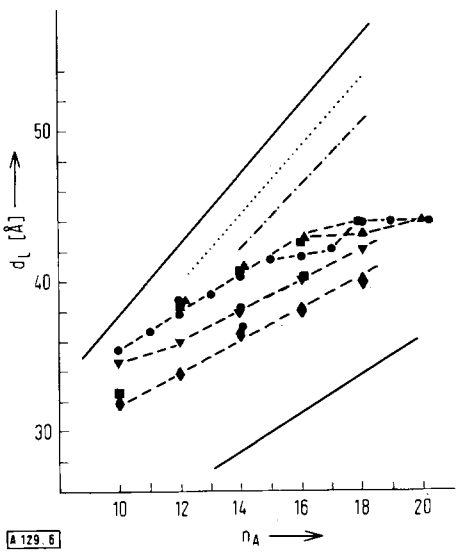

Fig. 6. Basal spacings d_L in the case of bimolecular films in gauche-block structures between silicate layers: dependence on the chain length of the alkanol (n_A). System as in Fig. 4 with ◆ $n_C=10$, ▼ $n_C=12$, ● $n_C=14$, ■ $n_C=16$, ▲ $n_C=18$; calculated values: —— monomolecular (bottom) and bimolecular (top) films, vertical alkyl chains; ·—· bimolecular chains inclined at 34° to the layer normal; .... bimolecular helical structures. For the term "gauche-block structure" see Section 5.1.

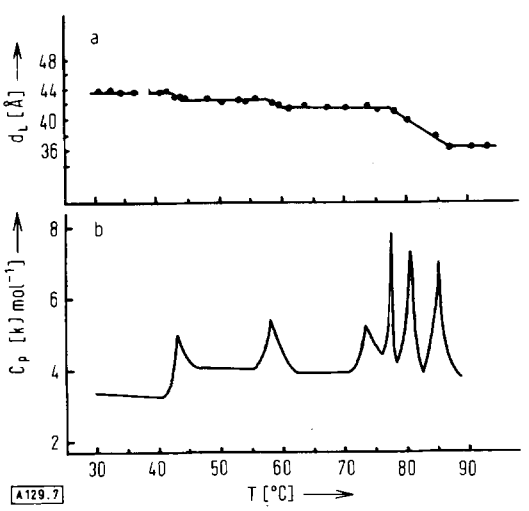

Fig. 7. Temperature dependence a) of the basal spacing d_L and b) of the specific heat C_p (referred to mol beidellite) for a bimolecular film between silicate layers (beidellite). System as Fig. 4 with $n_C=n_A=12$.

almost linearly with n_A. The transition temperature depends on the chain length (Fig. 14). It rises steeply with increasing chain length of the alkanol (n_A), but decreases again slightly for $n_A>n_C$.

3.2. Calorimetric Measurements

Measurements of the specific heat give an insight into the nature of the transition. This is demonstrated in Figure 7 for dodecylammonium-beidellite/dodecanol as an example. Within the series of the β-forms[*], the specific heat shows pronounced maxima just at the transition temperatures. The transition into the α_1-form takes place within the relatively large temperature range of almost 10°C and obviously passes through several steps, since four maxima are clearly apparent. (The stepwise transformation is probably the reason for the "quasi-melting" observed by *Stohrer* and *Noack*[51] in the nuclear resonance spectrum.) The striking point here is that, before the three sharp maxima, there is a maximum similar to the maxima observed at 42 and 60°C. Obviously a transition analogous to that at 42 and 60°C first takes place (β_3 into β_4!), but this is followed immediately by the transition into the α_1-form. Since the α_1-form contains less alkanol than the β_3-form, and at the transition point alkanol is expressed from the interlayer space, one of the maxima, probably the first of the three sharp ones, should be assigned directly to desorption of alkanol. The changes in the specific heat at the transition temperature show clearly that the individual forms are discrete phases which undergo transformation into one another. The form of the maxima indicates that the transitions are neither first-order phase transitions nor λ-transitions[49].

4. Conformations of Alkyl Chains in Lamellar Arrays

4.1. Possible Interpretations of the Observed Phase Changes

It could be assumed that the film thickness is reduced by an increasing tilting of the alkyl chains. In the β_1-phase the basal spacings are so large that they can be produced only by fully extended alkyl chains (all-*trans* conformation)

[*] To simplify the description the individual forms are here called the β- and α-forms (see Fig. 10); no uniform nomenclature for these and other forms of mono- and bimolecular films has yet been introduced [50].

perpendicular to the silicate layers. An argument against an oblique arrangement of the alkyl chains is the fact that the basal spacings of the β-phases always decrease by 1—1.2 Å regardless of the chain length. For the transition from the β- to the α-phases tilting of the alkyl chains cannot be excluded *a priori*.

Another possible explanation is based on the assumption that the chains are shortened by special types of conformational changes.

4.2. Kink-Isomeric Chain Conformations

Because of free rotation, an isolated alkyl chain can adopt a large number of rotational isomers. Fig. 8 gives information on the relationship between the *trans* position (rotation angle 0° at the energy minimum) of a C—C bond and two *gauche* positions with energies about 0.6 kcal/mol higher (2.51 kJ·mol^{-1}) [rotation angle *ca.* 112° (=g) and *ca.* −112° (=$\bar{g}$)[52, 53]]. In a lamellar structure of alkyl chains, such as is present in paraffins, polyethylene, and in mono- and oligomolecular films, however, only those conformations can occur

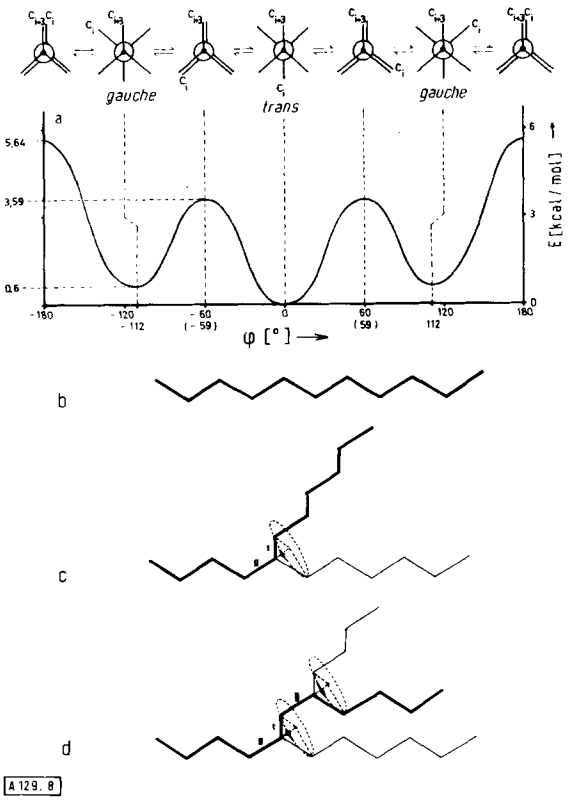

Fig. 8. a) Rotational potential (according to Refs. [54, 61]) and formation of kinks in alkyl chains; b) *all-trans* chain; c) chain with isolated *gauche* bond; d) chain with one kink.

in which the stretched nature of the chains is essentially retained. The most important group of conformations originate from regular sequences of *trans* and *gauche* bonds (Fig. 9). These conformations are called kinks: 2g1-kinks (conformation ... ttt*gtḡ*ttt ...), 2g2-kinks (... ttt*gttt*ḡttt ...), and 3g2-kinks (... ttt*gtḡtg*ttt ...). The formation of a kink in an alkyl chain shortens it by 1.27 Å[*] or a multiple thereof. (The symbol 3g2 means that the kink comprises three *gauche* bonds and

[*] This value applies to isolated alkyl chains. It may be smaller in alkyl chain lamellas, depending on the packing density [54].

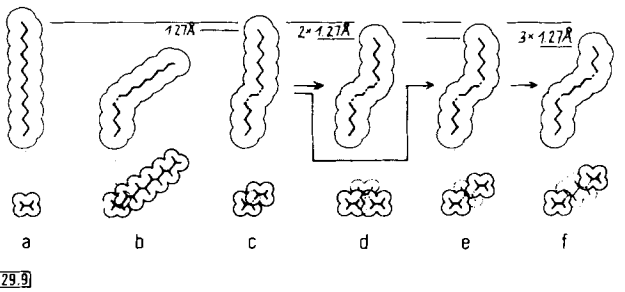

Fig. 9. Various types of kinks (after *Pechhold*) and alkyl chains with isolated *gauche* bonds. a) ttttttttttt (*all-trans*); b) tttgttttttt (isolated *gauche* bond); c) tttgtḡttttt (2g1 kink); d) tttgtḡtgtttt (3g2 kink); e) tttgtttḡtttt (2g2 kink); f) tttgtttttḡtt (2g3 kink).

shortens the chain by 2 × 1.27 Å.) In addition to the kinks, certain g-t sequences may occur throughout the whole chain; this gives rise to helical structures: 3_1-helix: gtgtgt... or gtḡtgtḡt...; 2_1-helix: nearly ...gggg...[55]. In the helical conformations kink-like defects may occur, *e.g.* in gtgtgt defects such as gtḡtgt or gtttgt, which can actually have negative defect energies[55], (Table 3).

Table 3. Defect energies of kinks in isolated alkyl chains and in alkyl chains in lamellar structures (after [52, 54, 55, 61]; 2g1 kinks see Fig. 9c).

	Defect energy [kJ·mol^{-1}]
2g1 kink in trans alkyl chains	
Kinks in isolated alkyl chains	5.0
Kinks as individual defects in a close packed alkyl chain lamella (as in polyethylene)	31.4 [a]
Kinks in a kink block [a] consisting of seven alkyl chains [b]	18.9 [a]
Kinks in a linear kink block [b]	21.0 [a]
Defects in helical chains	
ḡ-Defect in the gtgtgt helix	4.9
t-Defect in the gtgtgt helix	− 3.7

[a] Energetically most favorable figures [52].
[b] Cf. Fig. 10.

The concept of kinks is due to *Pechhold*[56], who showed in a number of papers that kinks occur as defects and as structural elements in paraffins, polymers, and polymer melts. Similar defects have been mentioned by *McMahon et al.*[57]. *Hosemann* has shown that the radiation-induced cross-linking of alkyl chains in polyethylene may be due to the presence of kinks, and that the paracrystallinity of polyethylene is connected with kink formation[58–60].

5. Kink-Block and Gauche-Block Structures

The decrease in the basal spacing in the β-phases by 1.0—1.2 Å (Fig. 10a) corresponds exactly to the shortening of alkyl chains by kinks. Approximately the value for an isolated alkyl chain is reached, since the packing density of about 24 Å^2/chain is considerably smaller than in paraffins and polyethylene (*ca.* 19 Å^2/chain) and the influence of neighboring alkyl chains is not so strong.

In the stability range of the β-phases the (00*l*)-reflections are rational up to high orders. This means that within a crystal all the layers have the same separation and the films are equally thick from layer to layer. The kinks cannot occur as isolated defects (Fig. 10b) but must be aggregated regularly into kink-blocks (Fig. 10c and 10d). In such kink-blocks the displacement caused by the kinks runs obliquely through

the film. These kinks are structural elements. In addition, isolated kinks can also occur as isolated defects.

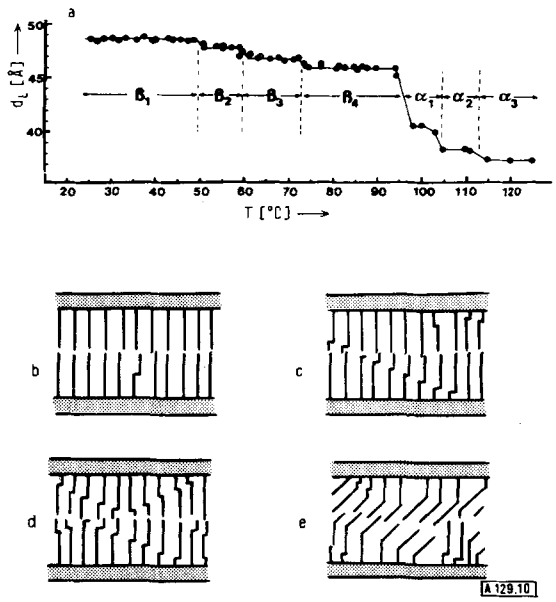

Fig. 10. Conformation of alkyl chains in a bimolecular film. a) Sequence of phases in bimolecular films between silicate layers (example $n_C = n_A = 14$, as in Fig. 4); b) *all-trans* block with a kink as an isolated defect; c) kink-block β_2; d) kink-block β_3; e) gauche-block.

The following phases may be distinguished (Fig. 10a):

β_1: All the chains are in the *all-trans*-conformation; kinks occur at the most as isolated defects and do not affect the layer separation (Fig. 10b).

β_2: A displacement due to ordered kinks runs through the whole bimolecular film. One kink occurs per pair of chains (that is two chains one above the other in the bimolecular film). *All-trans* chains (Fig. 10c) and pairs of chains with two kinks occur as isolated defects.

β_3: Two kinks occur per pair of chains, and either each chain of the pair contains one kink or one of the chains contains both kinks. Chain pairs with one kink and three kinks and, in very low concentration, *all-trans* chains occur as isolated defects (Fig. 10d).

β_ω: Contains pairs of chains with $\omega-1$ kinks and as isolated defects pairs with $\omega-2$, $\omega-3$... and ω kinks.

According to *Pechhold*'s calculations[61], the concentration of defects due to too few or too many kinks is of the order of 0.07 defects/chain. In addition, defects due to kinks in wrong positions may occur. Since the kinks are highly mobile in the chain direction[29, 62], these defects should easily disappear by displacement of the kinks along the chain.

5.1. Gauche-Block Structures

The film thickness of the high-temperature phases $\alpha_1, \alpha_2, \ldots$ cannot be interpreted as consistently as that of the low-temperature phases $\beta_1, \beta_2, \ldots$ In the first place it could be supposed that at the transition temperature so much alcohol is lost that the bimolecular film transforms into a monomolecular one. This is not the case. The film thicknesses lie clearly between the values calculated for bimolecular and monomolecular arrangements (Fig. 6).

It could be assumed that at the transition temperature $T_{\beta/\alpha}$ the state with a relatively low kink concentration passes into a state with a high kink concentration, similarly to what has been postulated for the rotational transformation of paraffins and for melts of polyethylene[56, 63]. This idea approaches closely the model for the liquid-crystalline phase of lipids due to *McCammon* and *Deutsch*[13]. However, the decrease in the film thickness could only be explained by kink densities that exceed the maximum possible number of kinks per chain. For simple helical forms (3_1-, 2_1-helices) the observed basal spacings are clearly too low. On the other hand, kinks of higher order ...$gt_x\bar{g}$... could occur. The necessary shortening of the chain requires relatively high values of x, *e.g.* for $n_A = 14$ each chain pair must contain two kinks with $x=3$ or one kink with $x=2$ and one with $x=4$, and so on. This leads to large parts of the chains being tilted to the layer normals. The above model can be considered only as a special case of the "gauche-block" model. In the gauche-block model it is assumed that relatively large parts of the chain are tilted to the layer normal because of a shifting of *gauche* bonds away from one another (Fig. 10e, and 11f). It is likely that gtg-conformations play an important role in the oblique arrangement of parts of the chains. According to *Pechhold*, these conformations are fundamentally involved in the meander-like structures in polymer melts[61, 63, 64]. Since the *gauche* bonds are not parts of kink-like conformations we use the expression "gauche-block structures".

In consequence of the loose packing the influence of the end-group interaction increases. It may be possible that some chains are inclined at 34° to the layer normal at their polar ends. This steric arrangement corresponds to an energetically particularly favorable arrangement of the NH_3 group and has been observed repeatedly[30, 98].

The packing density can be estimated by gravimetric measurements as about 1.3 alkyl chains per formula unit; it is therefore only slightly higher than the packing in monomolecular films (1.0 alkyl chains per formula unit). The area requirement per chain is about $2 \times 23.2/1.3 = 36\,Å^2$. Film thicknesses corresponding to gauche-block structures have also been measured in compounds such as niobates $K_4Nb_6O_{17}$[33] and alkylammonium polyphosphates[46, 65] with similar packing densities of the alkyl chains.

The proposed model is similar to the models used by *Whittington* and *Chapman*[66] and a model due to *McFarland* and *McConnell*[67]. In *Scott*'s statistical lipid model[12], gauche-block-like conformations are very important[12].

5.2. Influence of Chain Length on Kink-Block Formation

In the preceding sections systems with alkyl chains of the same length ($n_C = n_A$) and those with chains of different lengths in the alkylammonium ion and the alkanol molecule ($n_C \neq n_A$) were scarcely distinguished. The stepwise decrease in the film thickness by 1—1.2 Å and the transition into high-temperature phases occur in systems with alkyl chains of different lengths exactly as in the systems with chains of equal lengths. In systems with $n_A \neq n_C$ the changes of the basal spacings frequently appear to be even sharper, *i.e.* they appear to take place within a narrower temperature range.

The basal spacings shown in Figure 5 permit important deductions concerning the structure of the films. Bimolecular arrangements with vertical alkyl chains occur with alkyl chains of different lengths as well. In contrast to monomolecular films, however, there are several types of structures, depending

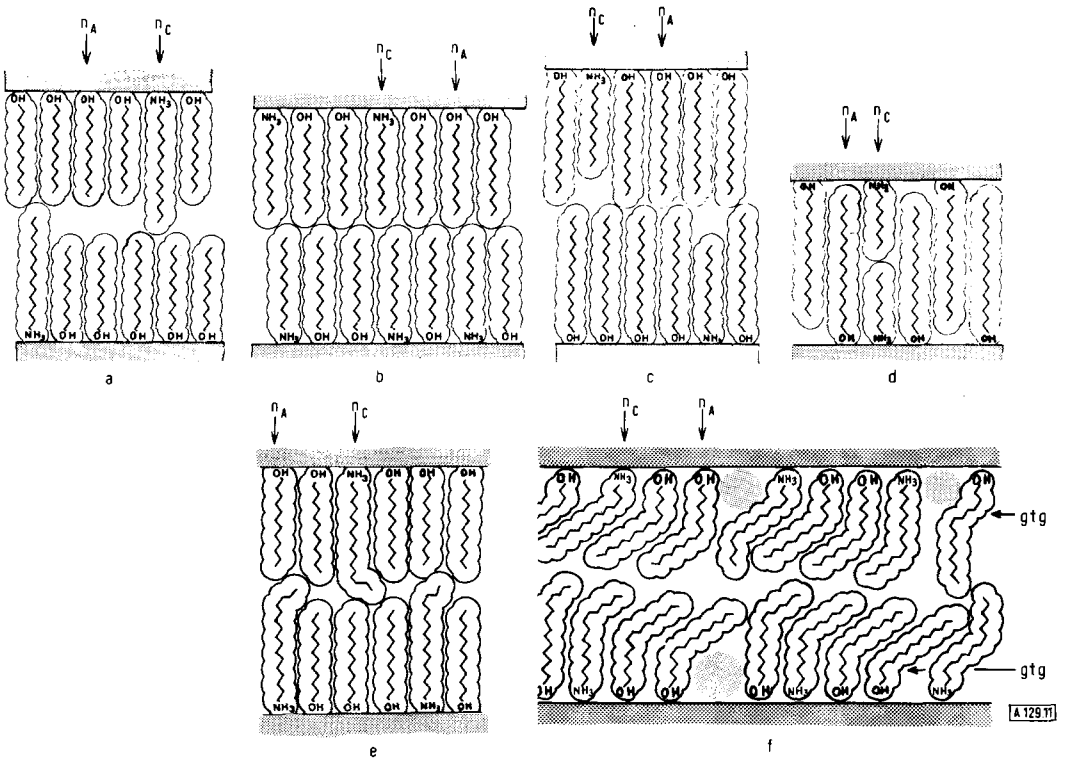

Fig. 11. Possible chain arrangements in bimolecular films. a) $n_A < n_C$, structure-determining pairs $\{n_C + n_A\}$; b) $n_A = n_C$; c) $n_A > n_C$, structure-determining pairs $\{n_A + n_A\}$; d) $n_A \approx 2n_C$, structure-determining pairs $\{n_C + n_C\}$; e) reduction of the vacancy volumes by kinks and isolated gauche bonds at the ends of the chains; f) gauche-block structure with partially filled cavities.

on whether short and short or long and long or short and long alkyl chains are opposite one another (Fig. 11). Two alkanol molecules (symbol $\{n_A + n_A\}$), two alkylammonium ions ($\{n_C + n_C\}$), or one alkylammonium ion and one alkanol molecule ($\{n_A + n_C\}$) may be one above the other. As Table 4 shows, the thickness of the bimolecular film is determined by the longest pairs that appear with greater frequency: for $n_A < n_C$ by the pairs $\{n_A + n_C\}$, for $n_A > n_C$ by the pairs $\{n_A + n_A\}$ (see Refs. [48, 49]). Holes (CH_2 vacancies) remain in the central region between the shorter chains (Fig. 11). In the case of very large differences in the chain length, the longer chains are shortened, probably by kinks or by *gauche* bonds at chain ends allowing the terminal methyl groups to move into the holes. In both cases the film thickness decreases by 1—1.2 Å (Fig. 11 e). In fact, differences of 1.1 Å or multiples of 1.1 Å are observed very frequently. Deviations can be caused by a different type of packing of the terminal methyl groups in the loosely-packed central region.

The films are sufficiently stable only when the region of the dense, undisturbed packing of the alkyl chains is sufficiently large. It must correspond to at least one alkyl chain with 12 carbon atoms on either side of the loosely-packed central region.

Table 4. Basal spacings of bimolecular films of alkylammonium ions and alkanol molecules of different lengths (n_C and n_A) between silicate layers (beidellite).

n_C	n_A	d_L [Å] obs.	$n_C = n_A$	d_L [Å] obs.	Model
10	12	41.7	12	43.4	$\{n_A + n_A\}$?
10	14	46.7	14	48.7	$\{n_A + n_A\}$?
10	16	50.8	16	52.5	$\{n_A + n_A\}$?
12	10	39.5	11	40.6	$\{n_C + n_A\}(\beta_2)$
12	12	43.4			$\{n_A + n_A\}(\beta_1)$
12	13	45.3	13	45.8	$\{n_A + n_A\}(\beta_3)$
12	14	48.3	14	48.7	$\{n_A + n_A\}(\beta_1)$
12	15	50.4	15	50.6	$\{n_A + n_A\}(\beta_1)$
12	16	52.0	16	52.5	$\{n_A + n_A\}(\beta_1)$
12	18	56.1	18	58.0	$\{n_A + n_A\}(\beta_3)$
14	10	40.9	12	43.4	$\{n_C + n_A\}(\beta_3)$
14	12	44.8	13	45.9	$\{n_C + n_A\}(\beta_2)$
14	14	48.7			$\{n_A + n_A\}(\beta_1)$
14	15	50.4	15	50.6	$\{n_A + n_A\}(\beta_1)$
14	16	52.4	16	52.5	$\{n_A + n_A\}(\beta_1)$
14	17	54.6	17	54.4	$\{n_A + n_A\}(\beta_1)$
14	18	57.0	18	58.0	$\{n_A + n_A\}(\beta_2)$
16	10	43.0	13	45.9	$\{n_C + n_A\}$?
16	12	48.4	14	48.7	$\{n_C + n_A\}(\beta_1)$
16	14	50.8	15	50.6	$\{n_C + n_A\}(\beta_1)$
16	16	52.5			$\{n_A + n_A\}(\beta_1)$
16	17	54.2	17	54.4	$\{n_A + n_A\}(\beta_1)$
16	18	58.0	18	58.0	$\{n_A + n_A\}(\beta_1)$
18	12	47.5	15	50.6	$\{n_C + n_A\}$?
18	14	52.3	16	52.5	$\{n_C + n_A\}(\beta_1)$
18	16	54.6	17	54.4	$\{n_C + n_A\}(\beta_1)$
18	18	58.0			$\{n_A + n_A\}(\beta_1)$

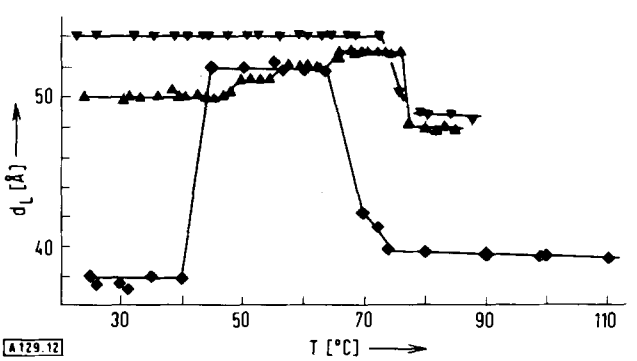

Fig. 12. Example of the sequence of phases in bimolecular films between silicate layers with large chain-length differences. System as in Fig. 4 with ◆ $n_C = 10$, $n_A = 18$; △ $n_C = 10$, $n_A = 24$, ▼ $n_C = 10$, $n_A = 26$ [69].

If the differences between the chain lengths are very large (*e.g.* $n_C = 10$, $n_A > 17$, $n_C = 14$, $n_A > 23$) other types of structure are observed (provisionally denoted as γ-phases). In many cases where $n_A \approx 2n_C$, alkanol molecules of approximately the same length are inserted between the $\{n_C + n_C\}$ pairs of alkylammonium ions: the structure becomes bimolecular with respect to the alkylammonium ions and monomolecular with respect to the alkanol molecules (Fig. 11d). With rising temperature additional alkanol molecules are taken up and β-structures are formed (Fig. 12). When the alkanol molecules are considerably longer than two alkylammonium ions opposite one another, structures with folded alkanol chains may occur. The stepwise increase of the basal spacing with rising temperature could indicate a shifting of the folds toward the chain ends in agreement with theoretical considerations[68].

6. Theory of Kink-Block and Gauche-Block Formation

6.1. Energy Data on Kink-Block Formation

It has been deduced from C_p measurements[49, 69], that the energy of formation of a kink in the kink-blocks is 0.7—0.8 kcal/mol (2.9—3.4 kJ·mol^{-1}) (Table 5). These values are not very accurate, since they were determined graphically from the C_p values, and the number of kinks per formula unit is not known precisely. Nevertheless, they show the order of magnitude, which is surprisingly low. In close-packed polyethylene the defect energy of a kinked alkyl chain is 7—11 kcal/mol (29—46 kJ·mol^{-1}); by aggregation of the defects it falls to half this value (Table 3)[54]. For an isolated alkyl chain the defect energy (1.3 kcal/mol) (5.4$_5$ kJ·mol^{-1}) is about twice the difference in energy between the *trans* and *gauche* states[52, 53].

The observed defect energy is still lower than this value. Since the basal spacing decreases on the formation of kink-blocks, for infinitely large layers the volume decreases and the packing density increases. The resulting gain in van der Waals energy leads to a slight decrease in the energy of kink formation. The effect should disappear with decreasing particle size. Nothing is yet known concerning its dependence on the particle size. The reduced defect energy is also revealed by the activation energy of kink relaxation, which is less than half of that in paraffins (4.7 kcal/mol as compared with 11–12 kcal/mol)[51].

The high defect energy in close-packed systems opposes the formation of a true kink-block in the alkylammonium-uvanite/alkanol complexes with dense packing of the alkyl chains. The defect energy for the formation of a kink in the nucleation step (more than 7 kcal/mol) in this system is obviously so high that nuclei which do grow into kink-blocks would appear only at temperatures above the transition point into the α-phase[99].

The change in entropy in the tetradecylammonium-beidellite/tetradecanol system is 2.3 cal·deg^{-1}·mol^{-1} (9.6 J·K^{-1}·mol^{-1}) for all three phase transitions (Table 5). *Pechhold*[61] calculated a value of 2.5 cal·deg^{-1}·mol^{-1} (10.5 J·K^{-1}·mol^{-1}), which is in very good agreement. The calculated values fall slightly for the three phase transitions; the experimental values are not sufficiently accurate to show such a change. In systems with alkyl chains of different lengths the transformation entropies are considerably higher.

Table 5. Enthalpies ΔH and entropies ΔS for kink-block and gauche-block formation (from C_p measurements on beidellite [49, 69]; the values are referred to 1 mol of beidellite).

T[°C]	Transition	ΔH [kJ·mol^{-1}]	ΔS [J·K^{-1}·mol^{-1}]
System: $n_C = 12$, $n_A = 12$			
42	$\beta_1 \rightleftharpoons \beta_2$	2.5	8.0
57.5	$\beta_2 \rightleftharpoons \beta_3$	3.4	10.0
74	$\beta_3 \rightleftharpoons \gamma_1$	3.4	9.6
78		2.9	8.4
81		5.8	16.3
85		5.8	15.9
System: $n_C = 14$, $n_A = 14$			
50 (48 [a])	$\beta_1 \rightleftharpoons \beta_2$	3.0 (3.1 [b])	9.6 (10.85 [a]; 9.47 [c])
60 (60 [a])	$\beta_2 \rightleftharpoons \beta_3$	3.0 (3.2 [b])	9.6 (10.48 [a]; 9.06 [c])
72 (69 [a])	$\beta_3 \rightleftharpoons \beta_4$	2.8 (3.3 [b])	9.6 (10.22 [a]; 8.26 [c])
System: $n_C = 14$, $n_A = 12$			
39	$\beta_2 \rightleftharpoons \beta_3$	5.0	15.9
50.5	$\beta_3 \rightleftharpoons \beta_4$	4.2	13.0
64 81	$\beta_4 \rightleftharpoons \gamma_1$	complicated behavior	

[a] Calculated [61]. [b] Calculated from ΔS [74]. [c] Calculated from ΔH [74].

6.2. The Cooperativity of Kink-Block Formation

Phase transitions in monomolecular films take place cooperatively in most cases[62, 70–72]. Kink-block formation is also a cooperative process[56, 61, 63, 64, 73, 74]. In a lamella of alkyl chains the probability of kink formation in one alkyl chain depends on the state of the neighboring chains. The probability is higher if a neighboring chain already contains a kink. The growth step, however, becomes appreciably faster than the nucleation step only if the kink is formed in a position favorable with respect to the neighboring chains. Steric effects play a fundamental role in this process. In the formation of a kink in a chain (nucleation step), the displaced part of the chain thrusts against the neighboring chains (Fig. 13), which give way by the formation of kinks. The reaction continues to the next chain (growth step), a kink in one chain being always displaced by two C atoms in relation to the neighboring chain. An ordered kink-block is formed.

The sharpness of the transition should increase with increasing chain length, since the cooperative length[71] and the dimensions of the kink-blocks become larger. In the case of the transitions within the kink-block phases this cannot be recognized particularly clearly from the steps in the basal spacings, while it is very pronounced on transformation in gauche-blocks.

The geometric prerequisites appear to be optimal in the case of the layer silicates: the packing density is about 24 Å^2, and the alkyl chains are arranged in a pseudohexagonal pattern. In the uranium micas the packing density is just as large, but because of the square arrangement of the alkyl chains no regular kink-blocks are formed. In the square arrangement the cooperative coupling remains one-dimensional, the growth step takes place only within individual rows of alkyl chains, and each row requires its own nucleation step[100].

So far there have been only a few attempts at a theoretical treatment of kink-block formation in bimolecular films. According to *Pechhold*[61], the gap compliance between the two monolayers contributes to cooperativity. This arises in view of the fact that even below the temperature of kink-block formation (in the $\beta_1 \rightleftharpoons \beta_2$ transition) a few chains contain

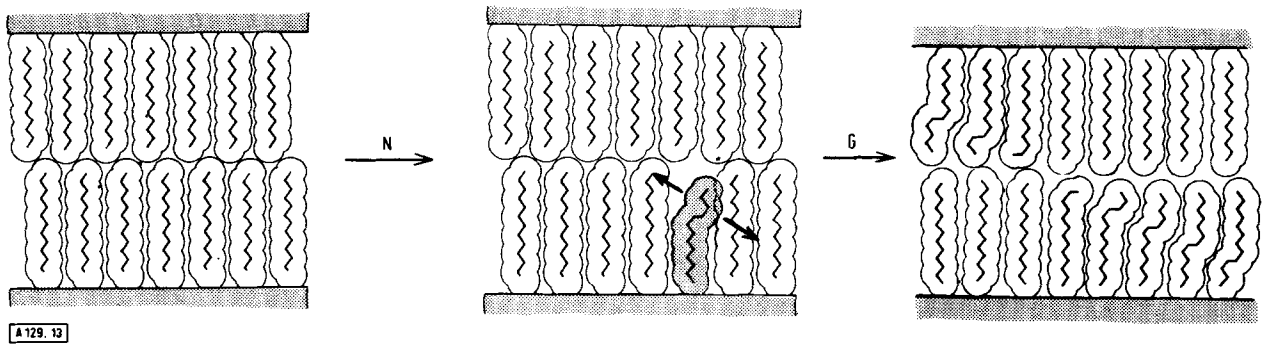

Fig. 13. Nucleation (N) and growth step (G) in the formation of kink-blocks.

kinks, and because of the rigid silicate layer the energy is raised by deformation of non-fitting chains. With $\Delta H = 0.83$ kcal/mol (3.48 kJ·mol^{-1}) and $\Delta S = 1.29$ cal·deg^{-1}·mol^{-1} (5.40 J·K^{-1}·mol^{-1}) for kink formation calculated and observed transition temperatures are in good agreement.

Baur[73-75] has made other attempts to treat the cooperative phase transitions in lamellas of alkyl chains. The calculations show that the formation of a sequence of kink-blocks in cooperative steps requires a sufficiently high aggregation tendency, *i. e.* definite values of the interaction energies between defect-free alkyl chains and alkyl chains with kinks as defects.

Because of cooperativity, the transitions in the series of kink-block structures do not correspond to first order transitions or to λ-transitions, as follows clearly from the C_p measurements (Fig. 7). As long ago as 1939—1942, *Harkins*[76, 77] and *Derivichian*[78] stated that phase transitions in monomolecular films may be of higher order[79]. *Baur* has calculated the multiplicity of changes in C_p on phase transitions in alkyl chain lamellas[73-75].

In our considerations so far the bimolecular film has been regarded as an individual alkyl chain lamella, although it is composed of two chemical individuals—the alkanol molecules and the alkylammonium ions. Since their ratio in the group of layer silicates investigated can vary from 1.8/0.2 = 9 to about 1.0/1.0 (for beidellite 1.57/0.43 = 3.7), this assumption can be checked. The same temperature dependence is observed in alkanol complexes of other layer silicates (vermiculites, montmorillonites): a sequence of β-phases occurs, which are transformed at higher temperatures into α-phases. Within the stability range of the β-phases the transition temperatures of the individual layer silicates are close to one another (Table 2). The ratio of alkylammonium ions to alkanol molecules has a clear effect on the transition temperature ($T_{\beta/\alpha}$) in the α-phase (Fig. 14), at which alkanol is expelled from the interlayer space. At a higher ratio of alkanol to ammonium ions than in beidellite, $T_{\beta/\alpha}$ is lower and is usually near one of the transition temperatures in the series of kink-block phases, *i. e.* instead of a kink-block a gauche-block is now formed. (This idea is supported by C_p measurements (Fig. 7), according to which at $T_{\beta/\alpha}$ a kink-block $\beta_{\omega+1}$ is formed which immediately changes into a gauche-block.) it is therefore possible, at least to a first approximation, to regard the bimolecular film of alkylammonium ions and alkanol molecules as a uniform alkyl chain lamella.

6.3. Transition into Gauche-Block Structures

The number of possible kink-block phases that are formed with rising temperature is limited. It is determined by an upper limit in the number of kinks in the structure-determining pairs of alkyl chains. (The β_ω-phase has $\omega - 1$ kinks per pair of alkyl chains.) This limiting value is smaller than the maximum possible number of kinks in the alkyl chain. It can be obtained in terms of the ratio C_K of the number of kinks to the number n of C atoms in the structure-determining pair of alkyl chains, and lies between 0.10 and 0.18[49]:

$$C_{K,\max} = 0.07 + 0.002\,n.$$

$C_{K,\max}$ gives the highest concentration of kinks in the β-phase.

The transition temperature $T_{\beta/\alpha}$ of the kink-block phase β_ω into the gauche-block phase α_1 has a maximum at $n_A = n_C$ (Fig. 14a). When $n_A \neq n_C$, the film contains holes (vacancies of CH_2 groups) and has lower transition points. The transition temperatures can therefore be represented as a function of the vacancy concentration (Fig. 14b). Again they lie on two straight lines for $n_A < n_C$ and $n_A > n_C$; for $n_A < n_C$ the $T_{\beta/\alpha}$ decreases strongly with increasing concentration of vacancies,

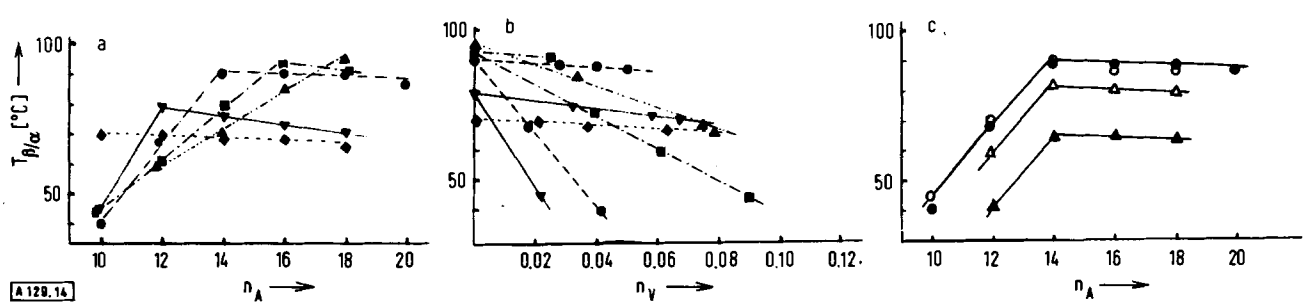

Fig. 14. Transition temperatures $T_{\beta/\alpha}$ of kink-blocks into gauche-block structures. a) As a function of the chain length of the alkanol n_A. System as in Fig. 4 with ◆ $n_C = 10$, ▼ $n_C = 12$, ● $n_C = 14$, ■ $n_C = 16$, ▲ $n_C = 18$; b) as a function of the concentration of vacancies n_V (vacancies/—CH_2); system as in a); c) with various ratios x of alkanol molecules and alkylammonium ions as a function of n_A for $n_C = 14$; ○ $x \approx 2.0$ (vermiculite); ● $x \approx 3.7$ (beidellite); △ $x \approx 4.6$ (Cyprus montmorillonite); ▲ $x \approx 6.1$ (Wyoming montmorillonite).

and this to an extent that is the greater, the shorter is the alkylammonium ion. For $n_A > n_C$ the transition temperatures fall slightly with the concentration of vacancies and are almost the same for $n_C = 14$ to 18. $T_{\beta/\alpha}$ is not a continuous function over the whole range, since the vacancies are not distributed uniformly over the film but are concentrated in the central region.

6.4. Structure of Bimolecular Films with Different Chemical Compositions

The structure and thermal behavior of bimolecular films depend on the type of polar molecules incorporated. So far it has not been possible to understand the complete variability of the film structure. If, for example, an alkan-1-ol is replaced by an alkan-2-ol, no typical kink-blocks appear. In the low-temperature forms the alkyl chains probably form simple helical conformations[55, 83]. At low temperatures, alkanediols give monomolecular films which, with rising temperature, pass into β-forms and finally into α-phases.

In connection with models of biomembranes the influence of double bonds in the alkyl chain[7] has been investigated in detail[80]. With the *cis* chains too kink-block phases are encountered at low temperatures. The *cis* chains are incorporated in the kink-blocks in the form of kink-like conformations *cis*-t-g (Fig. 15). They reduce the size of the kink-blocks and lower the temperatures of transition into gauche-block structures. If, in addition, alkyl chains of different lengths are present, and the concentration of double bonds is sufficiently high the transition temperature falls below 40 °C, so that gauche-block structures become stable in the physiological range of temperatures.

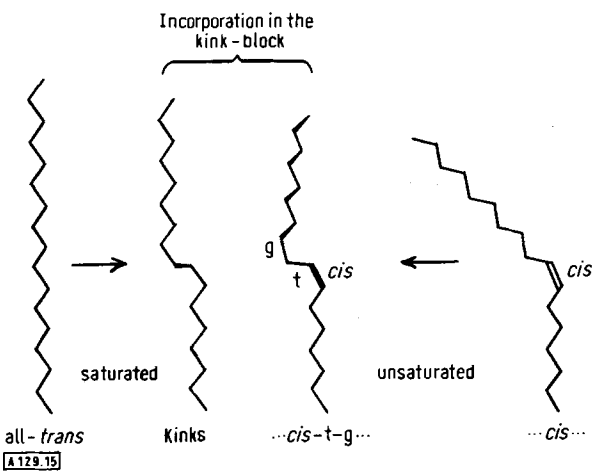

Fig. 15. Incorporation of *cis* unsaturated alkyl chains as *cis*-t-g conformers in kink-blocks. For comparison: transition of an *all-trans* chain into a chain with one kink.

Mono-, di-, and triglycerides[81] and glycerol ethers are also incorporated. At low temperatures, the high basal spacings correspond to structures similar to kink-blocks. At high temperatures, the structure changes into the α-form.

In relation to biomembranes, it is interesting to examine whether and how macromolecules can be incorporated in alkyl chain lamellas. These investigations are still in their initial stage, but in the case of simple linear macromolecules some characteristic results have already been obtained. Alkyl polyglycol ethers, for example, form bimolecular β- or α-phases with alkylammonium ions, depending on the degree of condensation[82]; on the other hand, polyvinyl alcohol is taken up with formation of monomolecular films having characteristic alkyl chain conformations[83]. The bimolecular structure is suppressed in favor of the formation of hydrogen bonds between the OH groups of the polyvinyl alcohol and the silicate layers. The results on the incorporation of proteins are still not very clear[84].

7. Conclusions

Only in the last few years has the phase change detected in lipid films by numerous methods of investigation[*] and even the generalized term of "chain melting" been clarified by model ideas. *Nagle*[79], *Seelig* and *Niederberger*[29], *Scott*[12], and *McCammon* and *Deutsch*[13] have related "chain melting" to the formation of *gauche* bonds and kinks in the alkyl chains. The concept of kink-block and gauche-block structures[48, 80] surpasses these ideas, since it permits a greater variability of phases and phase transitions. Important consequences for the structure of bimolecular films can be obtained. The investigations show that the alkyl chains in bimolecular films may still adopt *all-trans* conformations and be perpendicular to the layer even if the packing density is lower than in the crystalline compounds (*n*-alkanols, fatty acids, polyethylene with 19 Å²/chain). The lower limit lies at about 26 Å²/chain. The stability of the loose structure is probably due to less regular orientations of the planes of the carbon skeleton of the *all-trans* chains.

The films form kink-block structures in cooperative reaction steps by rotational isomerizations of the alkyl chains. The structural transitions can be initiated by raising the temperature. The formation of kink-block structures is associated with a packing density of about 22—25 Å²/chain. If an upper limit of the kink concentration is exceeded, the kink-blocks rearrange into gauche-blocks and the packing density of the chains falls to 33—40 Å²/chain.

The discovery that bimolecular films may contain high concentrations of holes (vacancies of CH_2 groups) must be regarded as another important conclusion. The maximum vacancy concentration is of the order of 0.05 vacancies/—CH_2, *i.e.* one vacancy to about 20 CH_2 units. In the model system, the vacancies are not distributed statistically but are concentrated in the central region of the bimolecular film. It is also not likely that a statistical distribution is formed. Even in polymer melts (with considerably higher vacancy concentrations) obviously no statistical distribution of the vacancies arises[85]. Films with vacancies change just as easily into kink-block and gauche-block structures as films without structural vacancies (alkyl chains with equal lengths); the transition temperatures depend on the vacancy concentration.

"Chain melting" of the lipids corresponds to the transition into gauche-block structures. The film thicknesses fall in a similar manner to the model system (*e.g.* by 10 Å in the case of dioctadecyllecithin[11] and 10.6 Å in the case of octadecylammonium-beidellite/octadecanol). The heats of transition are of the same order of magnitude: dihexadecyllecithin 8.7 kcal/mol, dioctadecyllecithin 10.7 kcal/mol[9], model system (referred to two alkyl chains per mol): 8—10 kcal/mol.

[*] For example ESR [24—26, 28], DNMR [18, 25], fluorescence measurements and dilatometry [27, 97], DTA [9—11, 97], and X-ray investigations [9, 11, 97].

Similar types of structure occur in biomembranes. Certainly, the order and structure in the kink-block phases of the lipid layers are not as high as in the model system, since a large number of different molecules is present. On the other hand the disturbance due to unsaturated alkyl chains with *cis* double bonds, for example, is not so high as might be assumed *a priori*. The *cis* chains do not interfere with the kink-block structure but adapt themselves by suitable conformations to the kink-block[80] (Fig. 15). However, they make the kink-blocks smaller and therefore reduce the temperature of transition into gauche-blocks.

The gauche-block structures should be of equal importance. Meanderlike gauche-block structures could actually determine the stress-strain behavior of muscle[87]. In gauche-block structures the less regular chain conformation and looser packing with larger cavities facilitates the incorporation of other molecules. The model in Fig. 11f resembles *Shah*'s concept: intermolecular cavities in mixed monomolecular films are filled with inserted molecules (Figs. 8 and 9 in Ref. [14]). According to the structural investigations reported by *Hitchcock et al.*[88], the long alkyl chains attached to glycerol are deformed by *gauche* bonds to such an extent that they form dense monomolecular films. Other molecules can be incorporated in these films only if cavities are produced by conformational changes in the alkyl chains. Possible structural changes are transitions into gauche-block structures.

In biomembranes, kink-block/gauche-block transitions may possibly be initiated by changes in the electrolyte system. The structure of the lipid region may also be changed by interaction with the membrane proteins[21-23].

The transitions between kink-block and gauche-block structures as a function of the chemical composition will affect the properties and reactions of membranes, such as permeability, transport processes[62], energy transformations[89], information processes, the conduction of stimuli in nerves, enzyme reactions, contact inhibition, and immune reactions. In these cases the hysteresis phenomena occurring in the kink-block/gauche-block transitions[48] should be of particular significance. A dynamic equilibrium may exist, between the kink-blocks and gauche-blocks similar to that proposed in the "fluid mosaic model"[22, 25, 90] between "crystalline" and "liquid-crystalline" regions.

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Detoxification of Automotive Exhaust Gases with Multifunctional Catalysts

By Wolfgang M. Weigert (deceased) and Edgar Koberstein[*]

Carbon monoxide, hydrocarbons, and nitrogen oxides can be simultaneously transformed into inoffensive substances on multifunctional catalysts. Consisting of noble metals or base metal oxides deposited on an inert support, these catalysts can be used in monolithic form or as granular packings. Compared with other methods of automotive exhaust detoxification, multifunctional catalysts are distinguished by incurring fuel savings.

1. Introduction

The ecological problems caused by the emission of automotive exhaust gases have already been surveyed in numerous publications[1-6]. Just how serious atmospheric pollution by the exhaust from internal combustion engines has become is apparent from Figure 1. Pollutants present in these exhaust gases are hydrocarbons—polycyclic arenes being the most serious offenders—carbon monoxide, nitrogen oxides, sulfur dioxide, sulfur trioxide, and solids. In the Federal Republic of Germany alone some 3650×10^3 t of carbon monoxide, 475×10^3 t of hydrocarbons, 815×10^3 t of nitrogen oxides, and 60×10^3 t of sulfur dioxide were emitted by motor vehicles in 1969.

Countries having high motor vehicle densities have introduced legislation stipulating limits for the emission of hydrocarbons, carbon monoxide, and nitrogen oxides and defining conditions for their measurement. Hence the motor industry

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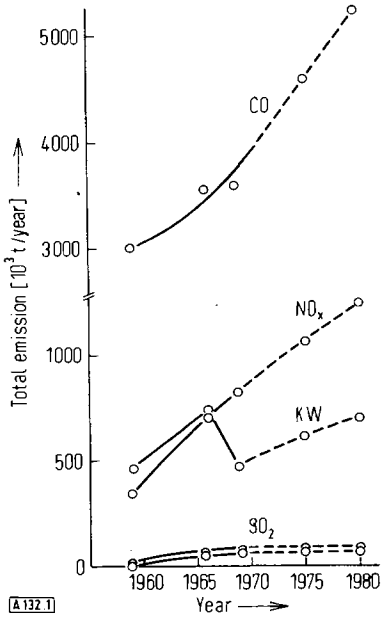

Fig. 1. Pollutants emitted by motor vehicles in the Federal Republic of Germany according to investigations by the Federal Ministry of the Interior [3]. HC = hydrocarbons.

is compelled to adopt suitable measures to comply with these stipulations. Differences in legislation from country to country and frequent changes in the requirements make this task difficult.

As an example, Table 1 lists the automotive exhaust standards presently valid in the USA and those expected in the future. By 1980 legislation is expected in the Federal Republic of Germany which will limit the pollutants in exhaust gases to one-tenth of the average values of 1969.

Table 1. US standards for automotive exhaust gases. Procedure: CVS-75 [14b].

Model year	Emissions standards [gram/mile]		
	Hydro-carbons	CO	NO_x
1975 California	0.9	9	2.0
1975 remaining USA	1.5	15	3.1
1976 California	0.9	9	2.0
1976 remaining USA	1.5	15	3.1
1977 California	0.41	9	1.5
1977 remaining USA	1.5	15	2.0
1978 [a]	0.41	3.4	0.40
1978—1982 [b]	1.5; 0.9; 0.41	15; 9; 3.4	3.1; 2.0; 1.0; 0.40

[a] According to the Clean Air Act (presently valid legislation; Muskie standards).
[b] Various proposed amendments to the Clean Air Act.

Several approaches to the reduction of pollutant emission have been examined with a view to satisfying these requirements.

Engine modifications are considered as a means of largely avoiding pollutant formation: these include the conception of radically different propulsion units for motor vehicles and changes in the design of the gasoline engine. More progress has been made in developing techniques for purifying the exhaust of conventional Otto cycle engines. In this connection, catalytic reactors converting the pollutants into the inoffensive gases carbon dioxide, nitrogen, and water have proved to be of great value. In particular, such reactors effect almost complete removal of polycyclic arenes (Fig. 2).

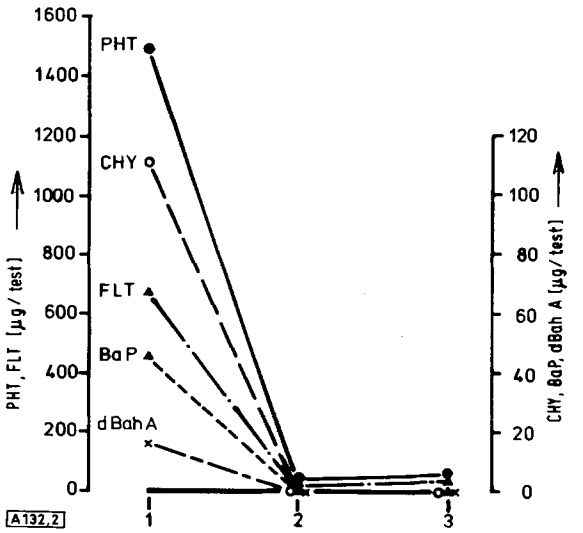

Fig. 2. Removal of polycyclic arenes from automotive exhaust gases by catalytic reactors. 1, without catalyst; 2, catalyst of type N; 3, catalyst of type E. PHT = phenanthrene; CHY = chrysene; FLT = fluoranthene; BaP = benzo[*a*]pyrene; dBahA = dibenz[*a,h*]anthracene.

In the USA several million vehicles have already been equipped with catalytic devices. Reports of American vehicle manufacturers about the performance of this new automotive component are positive. Hence catalytic exhaust detoxification can be regarded as having stood up to its first full-scale testing[7–9].

Development has not reached an end, however. Table 1 shows that increasingly stringent demands will be placed on exhaust purification in the future. Accordingly, new types of catalysts will have to be developed and it is with these that the present report is concerned.

2. Chemical Reactions in the Catalytic Detoxification of Automotive Exhaust Gases

The following overall reactions (1) to (9) occur during the transformation of pollutants emitted by engines into inoffensive compounds.

(1) $C_mH_n + (m + n/4)O_2 \longrightarrow m\,CO_2 + n/2\,H_2O$

(2) $CO + 1/2\,O_2 \longrightarrow CO_2$

(3) $H_2 + 1/2\,O_2 \longrightarrow H_2O$

(4) $NO + CO \longrightarrow 1/2\,N_2 + CO_2$

(5) $2\,(m + n/4)NO + C_mH_n \longrightarrow (m + n/4)N_2 + n/2\,H_2O + m\,CO_2$

(6) $NO + H_2 \longrightarrow 1/2\,N_2 + H_2O$

(7) $NO + 5/2\,H_2 \longrightarrow NH_3 + H_2O$

(8) $NH_3 + 5/4\,O_2 \longrightarrow NO + 3/2\,H_2O$

(9) $CO + H_2O \rightleftharpoons CO_2 + H_2$

From a thermodynamic standpoint all these reactions except (9) can go to completion; however, they require catalysts (for ΔG values see [10]).

An adequate supply of oxygen in the exhaust gas is essential for reactions (1) to (3). Several satisfactory oxidation catalysts have already been developed for these reactions. On use of these catalysts the nitrogen oxides were emitted largely

unchanged. So far, units containing oxidation catalysts have sufficed to meet the standards.

In view of the stricter legislation to be expected, however, methods must also be found for removing nitrogen oxides from the exhaust gases, *i.e.* for carrying out reactions (4) to (6). Since the reducing agents carbon monoxide, hydrocarbons, or hydrogen must be present for these processes, there should be no preceding oxidation reactions. It therefore seemed obvious to work with two separate catalysts (two-bed process). The first reactor contains a reduction catalyst which removes nitrogen oxides from the gas mixture. This is possible only if the exhaust gases comprise a reducing gas mixture, *i.e.* the engine must be driven in such a way that there is no oxygen in the exhaust. Prior to entering the second reactor containing the oxidation catalyst a secondary air supply to the exhaust gas is necessary (Fig. 3).

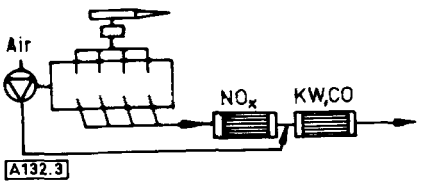

Fig. 3. Catalytic two-bed process. KW = hydrocarbons.

Although this technique considerably reduces the amount of pollutants in the exhaust gas, it nevertheless has its drawbacks. The two-bed solution places considerable demands on the equipment. Moreover, the usual catalysts are not sufficiently selective, so that part of the nitric oxide (up to 50 %) is reduced to ammonia according to eq. (7) and then partly reoxidized to nitrogen oxide according to eq. (8) in the second reactor.

In addition, the sulfur dioxide present in the exhaust gas is converted into sulfur trioxide. Emissions standards will probably be laid down for this compound in the near future. And finally, the two catalyst beds lead to considerable flow resistance, thus greatly increasing fuel consumption.

3. Multifunctional Catalysts

3.1. Action of Multifunctional Catalysts

The recently discovered catalysts which simultaneously mediate the oxidation and reduction reactions (1) to (6) represent a better solution (for their structure see Section 3.3). These multifunctional catalysts eliminate the three pollutants hydrocarbons, nitric oxide, and carbon monoxide, and are therefore also termed "three-way catalysts". However, the "three-way system" works satisfactorily only if it is operated within a certain limited oxygen partial pressure range in the exhaust gas.

The behavior of such catalysts is characterized with the aid of lambda curves. The conversion of the individual pollutants is plotted as a function of the air/fuel ratio characterized by the value λ (Fig. 4). λ is defined as the ratio of the amount of air introduced to the calculated air requirement for complete reaction. It is unity for stoichiometric conditions. The oxygen partial pressure in the exhaust also rises with increasing λ.

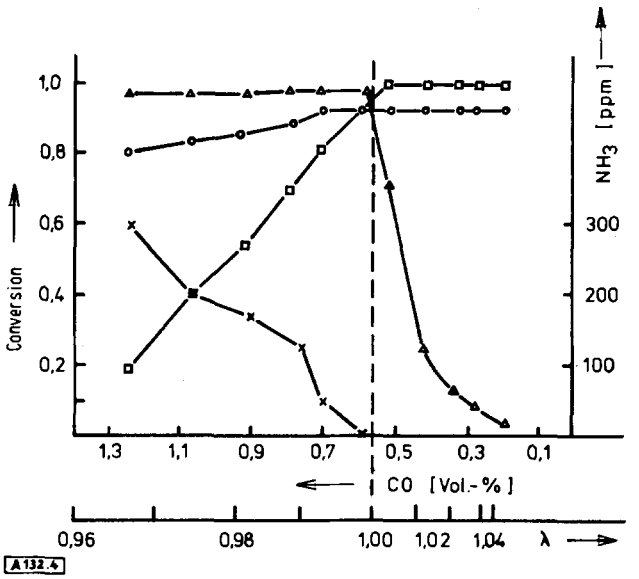

Fig. 4. Characteristic conversion curves lambda curves) for a multifunctional catalyst. □ CO, ○ hydrocarbons, △ NO_x, × NH_3.

Consideration of the conversion curves (Fig. 4) reveals an increase in conversion of hydrocarbons and of carbon monoxide with increasing λ. At $\lambda > 1$, a good catalyst permits practically complete conversion of the oxidizable pollutants.

Figure 4 refers to a catalyst that preferentially accelerates oxidation of hydrocarbons, which is generally desirable owing to the greater difficulty experienced in attaining the emissions standards for these pollutants. In the reducing range ($\lambda < 1$) nitric oxide is transformed almost quantitatively into nitrogen; at $\lambda > 1$ the conversion falls off rapidly.

The shape of the curve is a measure of the quality of a multifunctional catalyst. While the limited conversion in the range $\lambda < 1$ is attributable mainly to a stoichiometric deficit of oxygen and partly also to mass transfer phenomena under normal operating temperatures[10], the extent of the nitric oxide reactions in the range $\lambda > 1$ is restricted by the reaction kinetics and can therefore be influenced by the choice of catalyst. Reactions (4) to (6) are significant for removal of nitric oxide. As λ increases, reactions (1) to (3) begin to compete with reactions (4) to (6). For all catalysts so far known, the rate constants of reactions (1) to (3) predominate, and these reactions are therefore always preferred. This is also shown by Figure 5 which represents measurements performed with model gases in a laboratory reactor. Even on drastically increasing the carbon monoxide concentration, the conversion of nitric oxide is determined practically only by the oxygen partial pressure.

Thus only slight shifts of the nitric oxide conversion curves can be expected from the catalysts: however, these shifts are of considerable practical importance as they create a "lambda window", *i.e.* a λ range in which all pollutants simultaneously undergo almost quantitative reaction. Good three-way catalysts are also expected to suppress ammonia formation, which is shown to be feasible by Figure 4.

According to Figure 6, SO_2 is converted into SO_3 over multifunctional catalysts only at $\lambda \gg 1$. Thus the necessity of maintaining the window, *i.e.* of working at $\lambda \approx 1$, confers the added advantage of negligible SO_3 emission upon multifunctional catalysts as against conventional oxidation catalysts.

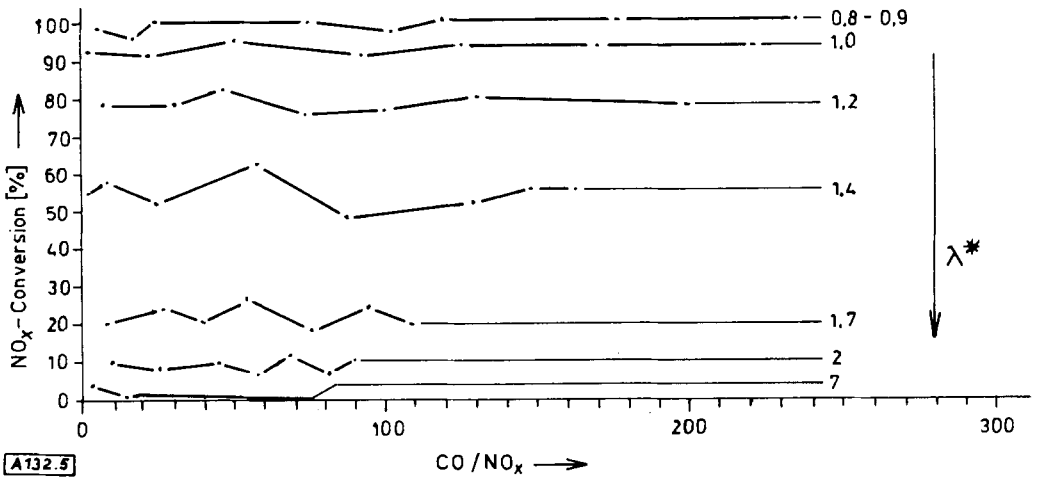

Fig. 5. Nitrogen oxide conversions at various oxygen concentrations in model gas mixtures at 700 °C. λ^* is a relative measure of the oxygen partial pressure. The CO/NO_x ratio is on a vol %/vol % basis. Space velocity 25000 h^{-1}.

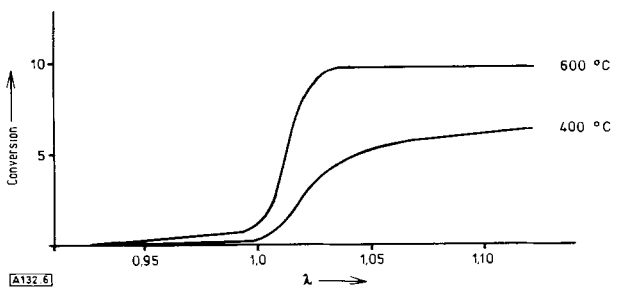

Fig. 6. Lambda curves for a multifunctional catalyst. The conversion of SO_2 into SO_3 was tested.

The conversion of pollutants also depends upon the temperature, a pertinent example being shown for $\lambda = 1.035$ in Figure 7. The temperature dependence of conversion is different for each pollutant. This is understandable because the activation energy E and frequency factor A will presumably differ in the Arrhenius equation

$$k_i = A_i \exp -E/RT$$

for reactions (1) to (6). Temperature effects of this kind can also play a role in practical application of the catalysts since widely fluctuating reaction conditions will attend the various operating states in a driving cycle.

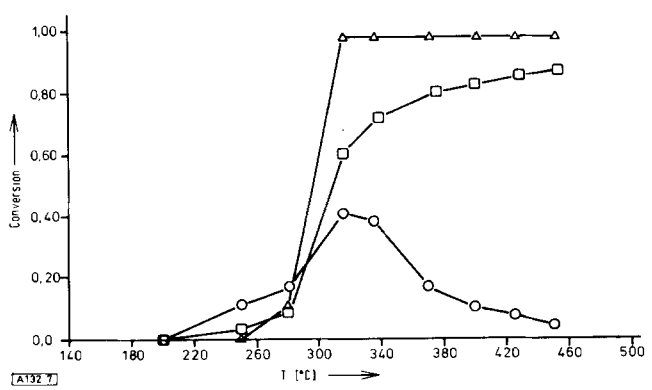

Fig. 7. Influence of gas temperature on the conversion of pollutants at a constant value of $\lambda = 1.035$. △ CO, □ hydrocarbons, ○ NO_x. Space velocity 70000 h .

A three-dimensional plot of pollutant conversions as function of λ and temperature furnishes typical surfaces for the various catalyst types. Figure 8 shows an example.

A knowledge of the pertinent motor characteristics permits choice and optimal adaptation of suitable catalysts on the basis of these results.

3.2. Methods of Maintaining the "Lambda Window"

The carburetors in present-day use lead to such extreme variation in the air/fuel ratio that the "lambda window" required for currently known multifunctional catalysts cannot be maintained. For this reason, modified carburetors on the one hand and controlled injection systems on the other have been developed which permit a considerably more accurate control of the value of λ for all kinds of operating conditions.

3.2.1. Fuel Injection

Fuel injection systems for Otto cycle engines have been in use for a considerable time. We distinguish between mechanically and electronically controlled systems.

Among the mechanically controlled devices special mention should be made of the "K-Jetronic" system[11]. In this approach the gasoline is continuously measured out *via* a fuel proportioning system which is mechanically controlled by an air meter located in front of the choke plate.

However, the fuel can also be measured out by electromagnetic injection valves whose opening times are determined by an electronic control device. In principle, several parameters are fed electrically to the control device and modify the opening times of the magnetic valves according to a given program. In the "L-Jetronic"[12], for instance, the engine speed and amount of air serve as input data.

3.2.2. Oxygen Sensor

On extension to include other control quantities these fuel injection systems can be used for catalytic three-way systems. As shown above the oxygen partial pressure plays a crucial role in the efficiency of multifunctional catalytic systems. Incorporation of an oxygen sensor in the exhaust pipe in front of the catalytic reactor permits measurement of the oxygen partial pressure which is used as an electrical control

signal in the control device. The oxygen sensor is an electrochemical oxygen concentration cell with a solid electrolyte (oxides with oxygen ion conduction). In this way a closed loop control be generated which guarantees an adequate "lambda window" also for varying operating conditions.

3.2.3. Modified Carburetors

Carburetors are modified with the intention of more exact control of the oxygen partial pressure. Approaches in which suitable amounts of additional air, again controlled by an oxygen sensor, are introduced may be cited for purposes of illustration[13]. The functioning and lifetime of the individual components, and especially the oxygen sensor, play a part in determining whether multifunctional catalysts are adopted, since it is only the overall system which is of interest in practice.

3.3. Composition of Multifunctional Catalysts

The demands placed on an automotive exhaust catalyst are exceptionally taxing. It must possess high mechanical strength, especially high compression strength and resistance to attrition. Above all, however, it must be thermally stable. In contrast to catalysts for chemical processes which operate at fairly constant temperatures, the exhaust gas catalyst must also display full activity under conditions of rapid and pronounced temperature fluctuations. It must detoxify the exhaust gases emitted under cold-start conditions, and it should not be damaged at excess temperatures such as may occur when the ignition fails.

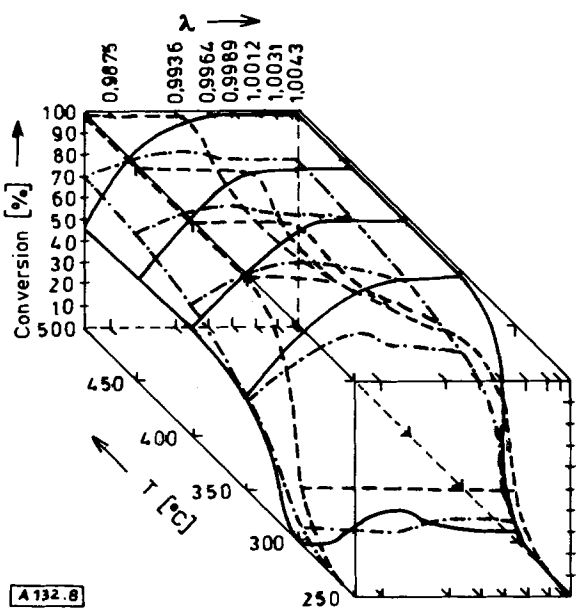

Fig. 8. Conversion curves of a multifunctional catalyst as a function of the temperature and the value of λ (catalyst characteristic). —— CO, -·-·- hydrocarbons, --- NO_x.

Figure 9 depicts a catalytic converter and multifunctional catalysts.

3.3.1. Support Material

Multifunctional catalysts are available as pellets or in monolithic form. A monolithic support consists of a single shaped unit penetrated by numerous channels. Parts of the cross sections of two catalysts having different kinds of monolithic supports are shown in Figure 10.

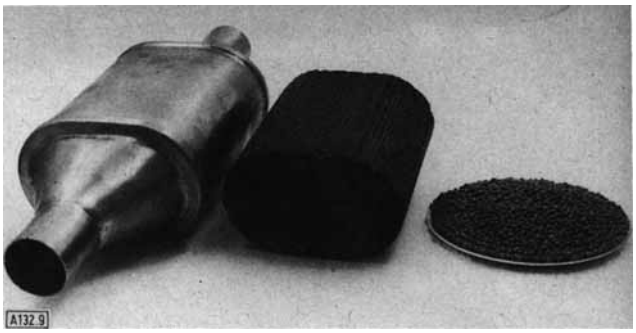

Fig. 9. Ready-for-use catalytic converter; monolithic catalyst; pelletized catalyst. Dimensions of converter: *ca.* 17 cm × 14 cm × 10 cm.

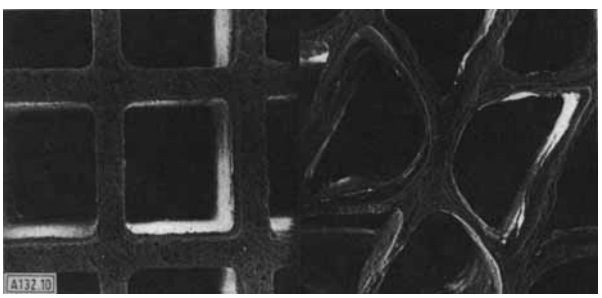

Fig. 10. Cross sections of monolithic catalysts (scanning electron micrographs).

The best material for ceramic supports has proved to be cordierite. This material has a favorable coefficient of thermal expansion, endowing the support with the good thermoshock properties required by the rapid temperature changes in automotive exhaust detoxification units. Depending upon the kind of engine and vehicle, the monolithic supports are used in various shapes and sizes, and with various channel cross sections and cell densities (number of channels per unit surface area).

The course of reactions (1) to (9) is also determined by mass transfer processes[10]. Hence the conversion of pollutants into inoffensive gases will also be affected by the cell density and the channel cross section of the monolithic catalyst material.

Supports for pellet type catalysts usually consist of spherical or extruded γ-alumina. The thermal stability and the resistance to attrition are generally not so good as with monolithic supports. Hence the use of pellet catalysts is nowadays limited to purification of exhaust gases from large motors since the thermal and vibrational stresses are comparatively smaller for such engines.

3.3.2. Active Coating

The catalyst support is coated with a layer of the active catalyst consisting either of base metal oxides or of noble metals. Active base metal phases are deposited directly on the ceramic supports. If a support is to be coated with noble metals then an intermediate oxide layer—in most cases also alumina—must first be applied.

Among the noble metal catalysts those containing platinum/rhodium/base metal phases have proved to be of utility.

Changes in the ratios of these components, the overall noble metal content, and the support material permit directed variation of the function of the catalyst.

Base metal oxide systems can also possess good multifunctional properties. The lambda curves are shown for such a catalyst in Figure 11. Base metal catalysts frequently contain nickel compounds. Relatively high gas temperatures are essential for the application of base metal catalysts.

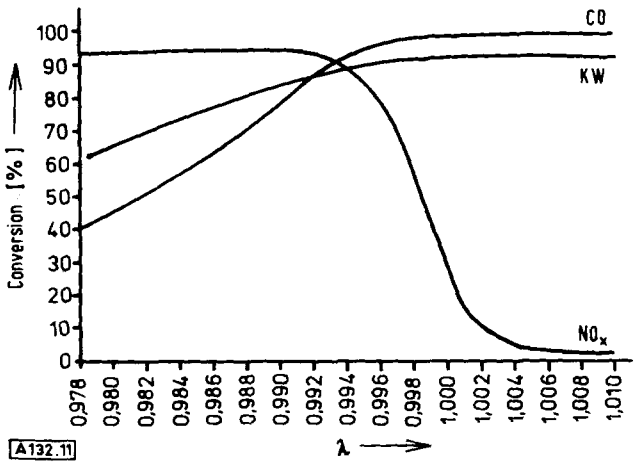

Fig. 11. Lambda curves for a multifunctional base metal oxide catalyst. KW = hydrocarbons.

In contrast, the noble metal catalysts also function at low temperatures, *i.e.* under cold-start conditions, but are easily poisoned by fuel additives and therefore require use of unleaded gasoline.

4. Use of Multifunctional Catalysts for Modified Processes

The above multifunctional catalysts permit extensive removal of all pollutants, even satisfying the most stringent emissions standards yet proposed (Muskie standards—Table 1). Operation within the "lambda window", *i.e.* around $\lambda = 1$, is a condition which in turn requires additional apparatus.

Now if higher emissions standards are to be tolerated for nitric oxide, as is also under discussion, then the motor can be operated with a larger λ window which would mean an inherent simplification of carburetion; an oxygen sensor would no longer be essential and the simpler K-Jetronic could be employed instead of the L-Jetronic system.

If the current US emissions standards were to stay, contrary to expectation, at the present levels, they could easily be met by the conventional oxidation catalysts. But even then, use of three-way catalysts would still have the advantage of requiring no secondary air supply.

Finally, mention should also be made of concepts directed at using multifunctional catalysts for the two-bed approach (reduction catalyst followed by oxidation catalyst, see Fig. 3). A multifunctional catalyst is employed for the reduction step and operated at $\lambda < 1$, but in the proximity of the stoichiometric point. This mode of operation avoids the formation of ammonia otherwise occurring in the double-reactor procedure.

5. Methods of Testing and Characterization of Catalysts

Just as important as emissions standards for pollutants are the standardized methods of testing the catalysts. The US government agencies prescribe the simulation of a particular driving cycle on a dynamometer corresponding to a typical cycle encountered in practice (Fig. 12). The exhaust gases emitted are collected in a constant volume sampler. Very exact measurements of emitted pollutants are possible in this way.

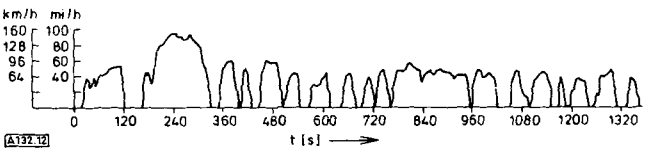

Fig. 12. CVS test 75, operating cycle.

This test is too involved and yet insufficiently specific for the development of catalysts since not only the catalyst but the entire system, including the engine, is estimated. Various shortened procedures have therefore been developed specifically for the characterization of catalysts. In a preliminary screening test model gas mixtures are used; automotive exhaust gases are used at a later stage.

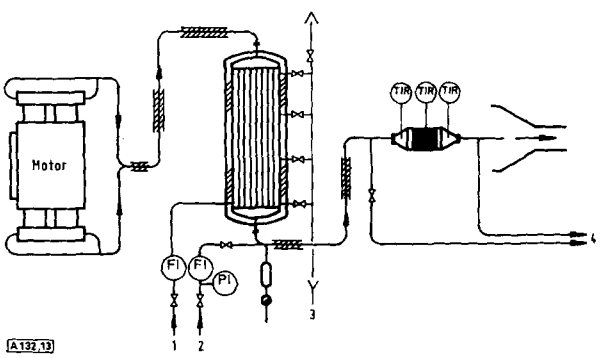

Fig. 13. Engine test for characterization of multifunctional catalysts. 1, cooling water; 2, air; 3, cooling water exit; 4, concerning analysis, FI, flow indicator; PI, pressure indicator; TIR, temperature indicator and recorder.

The approach described below has proved suitable for the development of multifunctional catalysts (Fig. 13). A stationarily operated engine is used which is loaded by an eddy-current brake; the fuel/air mixture can be precisely regulated by means of an electronic control device. The exhaust gases emitted by this engine are passed through a heat exchanger in which their temperature can be adjusted to any desired value and subsequently passed over the catalyst. The concentrations of hydrocarbons, carbon monoxide, nitrogen oxides, carbon dioxide, and oxygen are measured in front of and behind the catalyst with the aid of the instrumentation prescribed by the US tests[14]:

Hydrocarbons	– flame ionization detector
CO and CO_2	– ND infrared instruments
NO_x	– chemoluminesence instrument
O_2 (not stipulated)	– Magnos instrument (Hartmann & Braun)

Furthermore, the temperatures are registered immediately prior to entering and after leaving the catalyst and in its middle. All the parameters required for characterizing a catalyst, such as reaction temperature, concentrations of reactants, and space velocity, can be definitely and reproducibly adjusted with this equipment.

Characterization of three-way catalysts generally requires performance of the measurements described in Sections 5.1 to 5.3.

5.1. Conversion at Operating Temperature

Lambda curves are plotted, *i.e.* conversion curves for the pollutant components hydrocarbons, CO, and NO_x in the range $\lambda = 0.95$ to 1.05, whence the "lambda windows" (distance on the lambda scale between, for instance, 80% conversion of CO and of NO_x) and the intersection of the conversion curves for CO and NO_x can be deduced.

5.2. Low-Temperature Activity

In order to characterize its warm-up behavior, which is so important in practice, the catalyst is exposed to gases of increasing temperature, starting from 180°C, and the conversion measured.

5.3. Aging

In order to assess thermal damage the catalysts are subjected to heat treatment in a furnace and then tested in the same way to reveal any loss in activity or shift in the warm-up curve. A more realistic aging is accomplished in operation with an engine fed on a fuel/air mixture adjusted to give such a high CO concentration in the exhaust gas that the catalyst temperature increases to a predetermined maximum temperature of, *e.g.* 950 or 1000°C. At given time intervals the change in catalyst activity is checked by plotting a lambda curve and a warm-up curve.

6. Outlook

The methods adopted for detoxification of automotive exhaust gases in the future will depend upon the relevant legislation. If a reduction of nitrogen oxides is also prescribed then use of multifunctional catalysts appears attractive for several reasons. Requiring lambda values approximately equal to unity, this approach leads automatically to a very favorable fuel consumption and only slight SO_3 formation. Only one catalytic reactor is required and a secondary supply of air becomes unnecessary. However, these advantages are bought at the price of more stringent demands on the composition of the fuel/air mixture.

At the present state of the art, the catalytic three-way process is undoubtedly the most attractive possibility for extensive purification of automotive exhaust gases while maintaining favorable fuel consumption.

We are indebted to Dr. Hensel and Mr. Völker for their assistance.

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Orbital Correspondence Analysis in Maximum Symmetry[**]

By E. Amitai Halevi[*]

The use of Orbital Correspondence Analysis in Maximum Symmetry (OCAMS) for determining the allowed course of a reaction is described in terms of the familiar "A, S" notation. Several well known thermal and photochemical reactions are used as examples: Polyene cyclization; the fragmentation and dimerization of cyclobutadiene; $[_\pi 4 + _\pi 2]$ cycloaddition; the isomerization of Dewar-benzene. The relation of OCAMS to the classical correlation procedures of *Woodward* and *Hoffmann* and of *Longuet-Higgins* and *Abrahamson* is brought out, as are the sources of the occasionally contradictory predictions of OCAMS and of the classical procedures.

1. Introduction

Although the recognition that symmetry is an important factor in chemical reactivity goes back nearly half a century[1], it was only after the appearance on these pages of *Woodward* and *Hoffmann*'s classic paper[2] that considerations of symmetry became an essential component of the way nearly all chemists, organic chemists in particular, think about reaction mechanism.

Since then, developments in the field have been so rapid and so diverse that the proposal of yet another, formally different, approach to the subject[3] cannot but be greeted with reserve. Even after the theoretical soundness of the new method has been established[4], its proponent is apt to be asked:

1) Does it contain any genuinely novel features which take it so far beyond conventional procedures as to make it worth mastering?

2) If so, is it simple enough to learn and sufficiently easy to apply that it can hope to gain acceptance as a practical substitute for the conventional procedures, whenever the latter fail to yield unambiguous conclusions?

This report is an attempt to answer these two questions in the affirmative as regards Orbital Correspondence Analysis in Maximum Symmetry (OCAMS)[3,4]. Like the *Woodward-Hoffmann* approach and unlike methods that adopt a valence bond formalism[5,6] or take configuration interaction into account[7], and even though it can be used as a basis for state-correlation studies which include electron interaction[8], OCAMS is essentially a one-electron, Hückel molecular orbital procedure. Moreover, although orbital symmetry and molecular topology are evidently related, explicit consideration of topology[9,10] or aromaticity[11,12,6a] is avoided. Finally, no special weight is placed on the frontier orbitals[13,14], all of the occupied orbitals of reactant and product being afforded equal *a priori* status.

OCAMS is related to several aspects of *Bader*'s pioneering work[15], which has more recently been revived and extended[16,17], and also has certain features in common with the method newly proposed by *McIver*[18]. However, its closest relative is *Woodward* and *Hoffmann*'s orbital correlation procedure[19], which was formally justified by *Longuet-Higgins* and *Abrahamson* in terms of configuration correlation[20]. Accordingly, the procedure and findings of OCAMS will be repeatedly compared in the ensuing discussion with those of the WHLHA analysis which, in addition to being similar to it in outlook, is by far the best known of the earlier methods. For the latter reason too, the commonly used "S,A" notation will be adopted in this report instead of group-theoretical notation, which—although it is both more compact and less ambiguous—is unfamiliar to many organic chemists.

2. Orbital Correspondence Analysis: Polyene Cyclization

In their first communication[13], *Woodward* and *Hoffmann* discussed the cyclization of polyenes solely in terms of the symmetry properties of their highest occupied and lowest unoccupied molecular orbitals (HOMOs and LUMOs). In their second communication[19], they returned to the same reaction, which *Longuet-Higgins* and *Abrahamson* also used as a central example[20], but now considered correlations between all the molecular orbitals of the reactant and product that might be involved in the reaction. The present discussion will therefore begin with a brief review of the familiar WHLHA analysis of the cyclization of *s-cis*-butadiene to cyclobutene, which will facilitate the exposition of OCAMS that is to follow.

2.1. WHLHA Correlation Procedure

It is seen at the top of Figure 1 that the reactant *(1)* and product *(2)* have two symmetry elements in common: A twofold rotational axis C_2 and a mirror plane m which bisects the molecule. *(1)* and *(2)*, which belong to the symmetry point group C_{2v}, each also has reflection symmetry in the molecular plane, but this third symmetry element, which we might denote by m', is discarded as "useless", since it does not bisect bonds made or broken in the reaction[2].

In the order to convert *(1)* into *(2)*, the two methylene groups must each be rotated by 90°, but if they are twisted separately, all molecular symmetry is destroyed along the reaction path. By carrying out the two rotations in a concerted manner, either C_2 or m—but not both—can be retained as a symmetry element; which one is retained depends on whether the two methylene groups are rotated in the same (conrotation) or the opposite sense (disrotation). Two correlation diagrams are then set up, one for each mode. In each, the symmetry properties of the molecular orbitals are specified with respect to that symmetry element which is retained along the reaction path, *i.e.* C_2 in the conrotation (Fig. 1a) and

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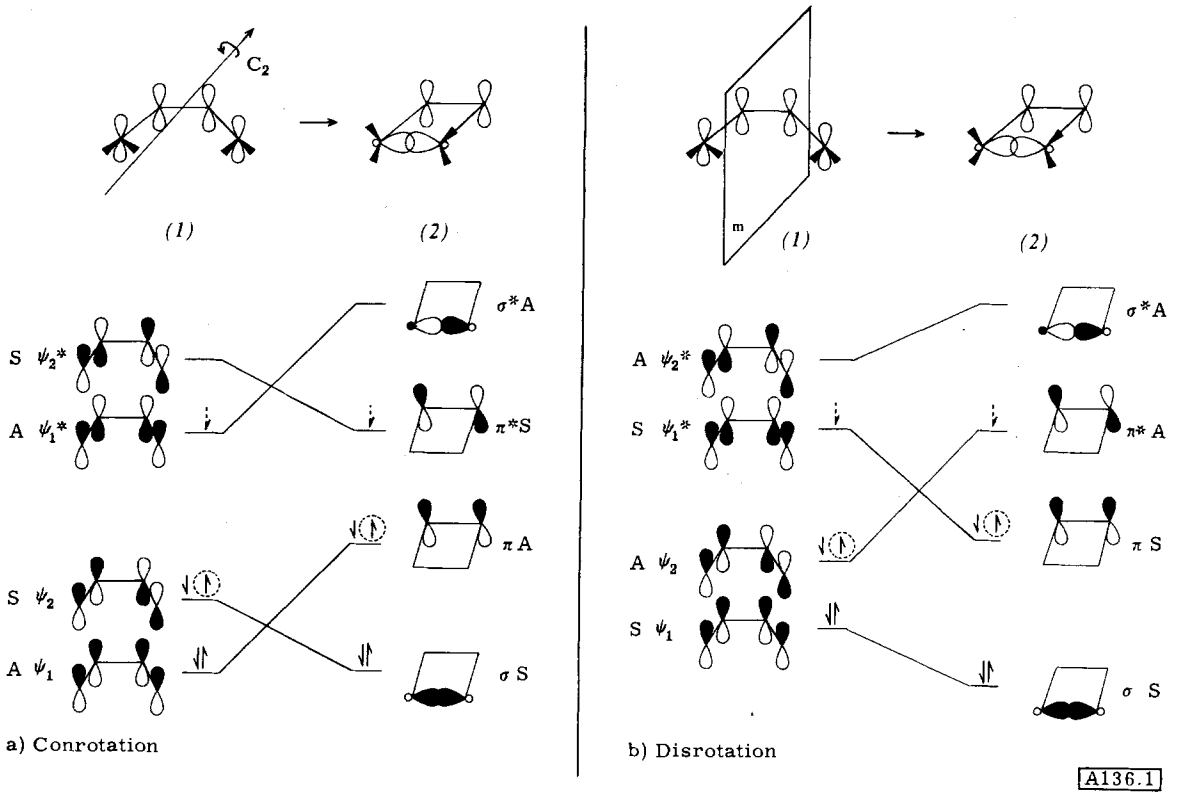


Fig. 1. WHLHA correlation diagrams for cyclization of *s-cis*-butadiene.

m in the disrotation (Fig. 1 b). The stacking of the molecular orbitals in order of increasing energy, which is of course the same in both diagrams, is self-evident, as is their characterization as S (symmetric) or A (antisymmetric) in each of the two modes. Correlation lines are drawn between orbitals of similar symmetry, care being taken not to violate the quantum mechanical rule that prevents two lines correlating pairs of orbitals with the same symmetry from crossing. (Non-crossing rule.)

Figure 1 a shows that the two orbitals which are doubly occupied in the ground state of the diene correlate with the two occupied orbitals of the product along a conrotatory pathway. In terms of configuration correlation, the ground-state configurations of reactant and product correlate with each other: $\psi_1(A)^2\psi_2(S)^2 \Leftrightarrow \sigma(S)^2\pi(A)^2$. From the viewpoint of either orbital or configuration correlation, the thermal, ground-state, reaction can be characterized as conrotatorily "allowed". In contrast, Figure 1 b shows thermal cyclization along the disrotatory pathway to be "forbidden", whether one invokes the orbital cross-correlation between occupied and unoccupied orbitals, familiarly referred to as a "HOMO-LUMO crossing", or the failure of the ground-state configurations to intercorrelate: $\psi_1(S)^2\psi_2(A)^2 \not\Leftrightarrow \sigma(S)^2\pi(S)^2$.

Before going on to the excited state reaction, we must recognize that no one-electron analysis can distinguish between singlet and triplet states having the same orbital occupancy. In anticipation of our discussion of open shell reactions (Section 5) the arrows in Figure 1 representing spin have been drawn so as to suggest a triplet state reaction. At this stage, however, the excited state reaction is discussed as if it were the same for both multiplicities.

Returning to Figure 1 a, we focus our attention on the excitation from ψ_2 (HOMO) to ψ_1^* (LUMO), which causes each to be singly-occupied. Since singly-occupied ψ_2 correlates with doubly-occupied σ rather than with singly-occupied π or π^*, the conrotatory excited state reaction is "forbidden", a conclusion borne out by the lack of configuration correlation between the lowest excited states: $\psi_1(A)^2\psi_2(S)^1\psi_1^*(A)^1 \not\Leftrightarrow \sigma(S)^2\pi(A)^1\pi^*(S)^1$.

From Figure 1 b we see that, thanks to the cross-correlation between the singly-occupied HOMOs and LUMOs and the fact that the doubly-occupied ψ_1 and σ are both S, or —equivalently and more compactly—because: $\psi_1(S)^2\psi_2(A)^1\psi_1^*(S)^1 \Leftrightarrow \sigma(S)^2\pi(S)^1\pi^*(A)^1$, the photochemical reaction is "allowed" along a disrotatory pathway.

For the purpose of comparison with OCAMS, we note two important features of WHLHA:

1) Not all the symmetry elements common to reactant and product are used in the analysis. Specifically, reflection in the molecular plane m' has been dismissed as "unimportant".

2) Reaction paths corresponding to different ways of reducing symmetry are analyzed separately. The symmetry-breaking motion (here a conrotation or a disrotation) is not considered explicitly; rather, its consequences are explored by characterizing each orbital with respect to the symmetry elements that are retained after the distortion has been applied, in our example either C_2 or m but not both.

It will now be shown how OCAMS elicits the same information about polyene cyclization in a rather different way, *i.e.* by investigating the symmetry properties not only of the molecular orbitals but also of the symmetry-breaking motions, and by ensuring that their symmetry is specified with respect to all, not just an arbitrarily selected few, of the symmetry elements common to the reactant and product.

2.2. Direct Correspondence

We first examine the symmetry of the MOs with respect to both of the "important" symmetry elements. Figure 2 which

is essentially a superposition of Figures 1a and 1b, shows that, in the original geometry, the MOs fall into four types: (1) SS—symmetric with respect to both C_2 and m; (2) AA—antisymmetric with respect to both; (3) SA—symmetric with respect to C_2 but antisymmetric with respect to m; and (4) AS—*vice versa*. Orbitals of the first two types evidently lie in the molecular plane and are symmetric to reflection in it m′, whereas those of the third and fourth type have a node in the molecular plane and are thus antisymmetric to m′. Clearly, types (1) and (2) are σ-orbitals whereas types (3) and (4) are π-orbitals. If we wished to make the π or σ nature of each orbital explicit, we might add a third A or S, referring to the symmetry with respect to m′, to those for C_2 and m. Then, AS would become ASA, SA would be SAA and the two of σ type would be SSS and AAS. In C_{2v} symmetry, this overspecification is unnecessary, the π or σ character of each orbital being evident without it. The symmetry properties with respect to C_2, m and m′ are fully determined in terms of any two of them[21].

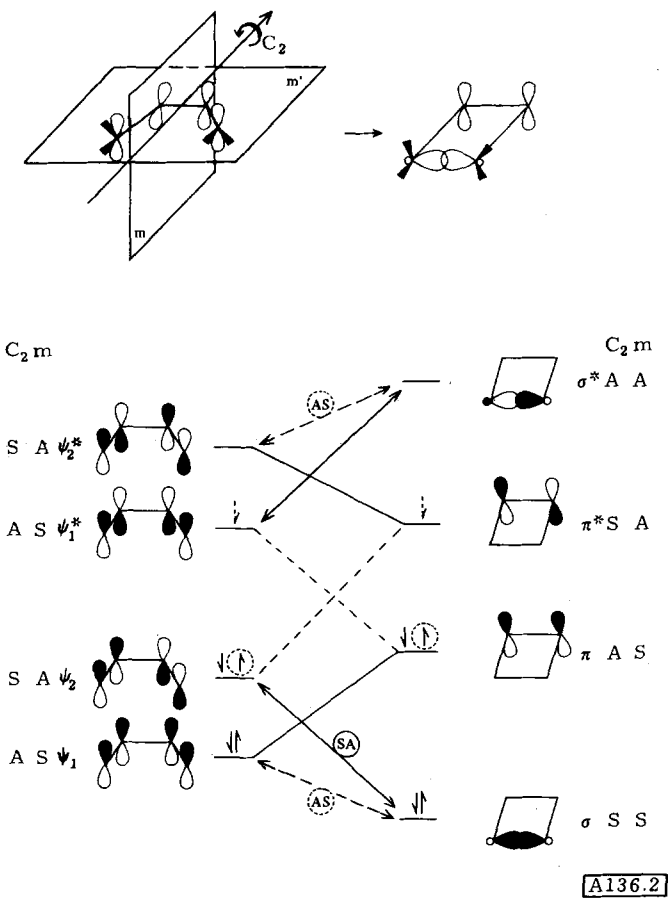


Fig. 2. Correspondence diagram for cyclization of *s-cis*-butadiene.

Direct correspondence
Conrotatory
Disrotatory
Induced correspondence
SA
AS

Two of the four π-orbitals of butadiene can be brought into *direct correspondence* (SA↔SA; AS↔AS) with those of cyclobutene, ensuring that two reactant orbitals could correlate with two of the product without any reduction of symmetry at all. Moreover, if the symmetry does happen to be reduced by a conrotation or a disrotation, these pairs of orbitals could still correlate with each other, since their symmetry properties are identical with respect to both C_2 and m and would remain so with respect to which ever one of them is retained along the pathway.

Note, however, that π corresponds with both ψ_1 and ψ_1^* while π^* corresponds with both ψ_2 and ψ_2^*, whereas, along any reaction path, each orbital of the product can correlate with only one reactant orbital. Therefore, a correspondence line between orbitals of the same overall symmetry, *i.e.*, one that denotes a direct correspondence, merely indicates that the two orbitals *can* correlate whether or not the symmetry of the reacting system is reduced, but not whether they *will* correlate. The eventual orbital correlations, which differ for different reaction paths, can hardly be ascertained before the nature of the pathway has been determined[22]. Since the two σ-orbitals, notably σ(SS) which is doubly-occupied in both the ground and first excited state, are left out of all the direct correspondences, it is obvious that cyclization cannot take place unless symmetry is reduced, and the onus is placed firmly on the requirement that two electrons be taken from a π-orbital of butadiene and delivered to a σ-orbital of cyclobutene.

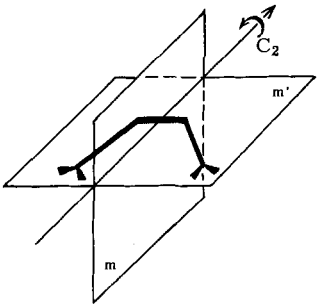
2.3. Induced Correspondence

We must therefore find a way of inducing a correspondence between one of the doubly occupied π-orbitals of butadiene and the bonding σ-orbital of cyclobutene. For this purpose a procedure is borrowed from the way spectroscopic selection rules are deduced, and reformulated as follows: *Correspondence between two orbitals, both of which are either symmetric or antisymmetric with respect to a given symmetry element, can only be induced by a displacement which is symmetric with respect to that element. If one orbital is symmetric and the other is antisymmetric with respect to a given element, they can be brought into correspondence only by a displacement that is antisymmetric with respect to that element.*

For example, in order to induce a correspondence of the type AS↔SS, the system must be distorted along a coordinate that is antisymmetric with respect to C_2 but symmetric with respect to m, *i.e.* one that can be represented as AS. Alternatively to induce the correspondence SA↔SS (and/or AS↔AA) a motion of type SA is called for.

The specification of the symmetry properties of displacements, which is common practice in vibrational spectroscopy, is less familiar to organic chemists than the similar characterization of molecular orbitals, but it is no more difficult. Figure 3 shows a number of symmetry coordinates, *i.e.* coordinates that are either symmetric or antisymmetric with respect to all the symmetry elements of the system, by means of arrows depicting the motion of the individual atoms. If, on application of a given symmetry coordinate—say *m*—to the molecule, all the arrows go into themselves or into arrows identical with them in length and direction, the coordinate is S with respect to m. If m takes all the arrows into arrows of the same length pointing in the opposite directions, it is A. If it does neither, the displacement depicted is not a symmetry coordinate[23].

The correspondence diagram in Figure 2 can now be completed by adding the required induced correspondences (denoted by two-headed arrows labeled according to the symmetry of the inducing coordinate) to the direct correspondences between occupied orbitals. For the ground-state reaction, ψ_2(SA)↔σ(SS) clearly calls for an SA distortion, which Figure



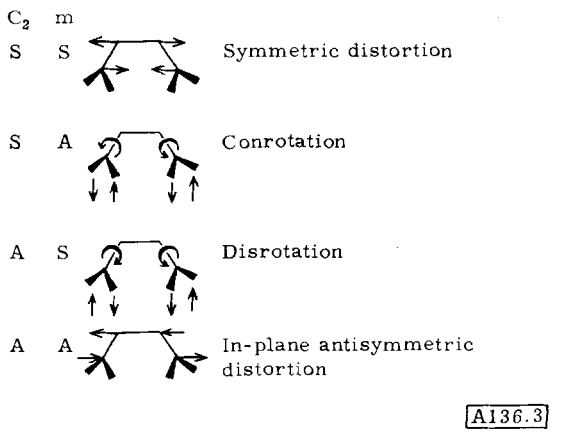


Fig. 3. Some symmetry coordinates of *s-cis*-butadiene.

3 identifies to be a conrotation. Similarly, in the excited state reaction, a disrotation, which Figure 3 characterized as AS, is suitable for inducing the required correspondence: $\psi_1(AS) \leftrightarrow \sigma(SS)$. The agreement with the WHLHA predictions becomes all the more evident when it is noted that the set of correspondences, direct and induced, selected by a conrotation (full lines in Fig. 2) reproduce the correlation lines of Figure 1 a, whereas the disrotatory correspondences (dashed lines in Fig. 2) similarly reproduce Figure 1 b.

2.4. Has Anything Been Gained?

Since the predictions of OCAMS are identical with those of WHLHA for polyene cyclization, we shall have to go on to less simple reactions in order to illustrate the greater predictive power of the former. Several marginal advantages are, however, already perceptible.

a) The driving force for the reaction, and the factor governing its stereochemistry in both the thermal and photochemical reactions, is clearly identified to be formation of a σ bond from a pair of electrons originating in a π-orbital. This point is obscured in the conventional analysis, in which π and σ orbitals, each of which can be either S or A with respect to C_2 or m, are not formally distinguished from each other.

b) The justification for regarding certain symmetry elements as more important than others becomes clear. C_2 is the essential symmetry element for a conrotation, as m is for a disrotation, because it is the one diagnostic symmetry element that is not destroyed along the reaction coordinate. The lesser importance of m' in this reaction, does not depend on its failure to bisect bonds made or broken in the reaction, but rather on the fact that it is not retained along either pathway leading to polyene cyclization. In other reactions, to be discussed in subsequent sections, it can be put to good diagnostic use, whether or not it bisects bonds made or broken[24].

c) By characterizing the orbitals fully before symmetry is reduced, OCAMS eliminates the necessity for choosing the pathway by intuition or by trial and error. This feature can be particularly important in reactions for which the possible pathways are less intuitively obvious than they are in our example, and where a possible reaction path might therefore conceivably be overlooked.

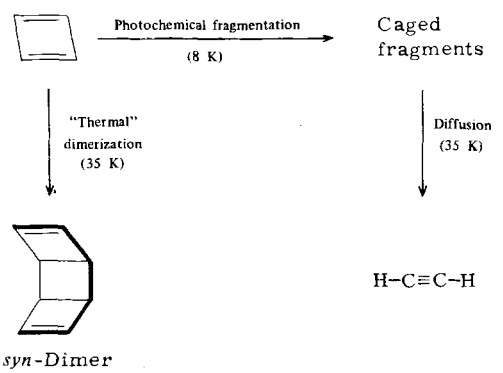
3. Maximum Symmetry: Reactions of Cyclobutadiene

Chapman et al., having produced cyclobutadiene photochemically at very low temperatures in an argon matrix, found it to react as summarized in Scheme 1[25]. These reactions will be used to demonstrate the advantages of two aspects of maximum symmetry:

a) Allowing a preferred reaction path to emerge from a correspondence diagram, rather than choosing several possible pathways by intuition and analyzing them individually for "allowedness".

b) Retaining all the symmetry elements that are necessary to characterize the system fully, rather than arbitrarily selecting several of them as more important than others.

Scheme 1.



3.1. Fragmentation of Cyclobutadiene

The ground state of cyclobutadiene is almost certainly a planar singlet, but whether it is rectangular as required by Hückel theory or whether electron correlation is strong enough to preferentially stabilize it in the square geometry, is less clear[26,27]. In either case, fragmentation to two acetylene molecules necessarily distinguishes between the bonds that are to be ruptured and those that will remain intact in the product. The "reactant" can thus be regarded either as one of the two equivalent isomers of cyclobutadiene, or—if the lowest singlet is indeed square-planar—as having been distorted slightly in the direction of eventual fragmentation.

We begin once more with the WHLHA approach, and characterize the molecular orbitals in Figure 4 on the basis of the two "important" mirror planes, m_1 and m_2, that bisect the π-bonds being formed and the σ-bonds being broken respectively. The four occupied orbitals and the lowest unoccupied orbital (which is the only one shown in the figure) on either side are ordered on the basis of the usual considerations: σ-interactions are stronger than π-interactions, the energy

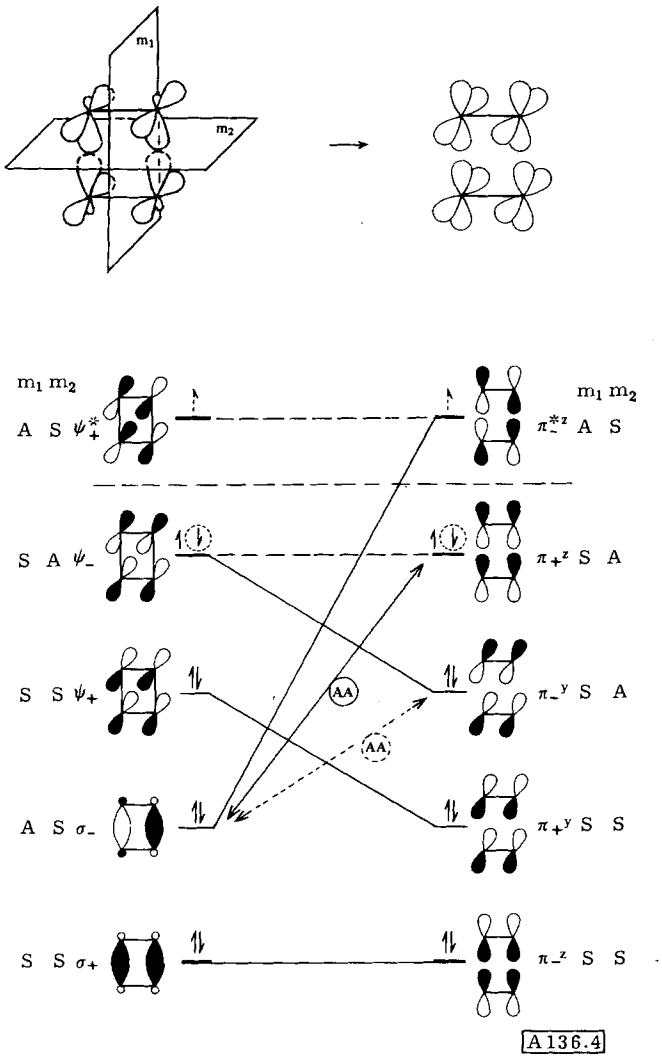


Fig. 4. Preliminary analysis of fragmentation of cyclobutadiene (higher unoccupied orbitals not shown).
Full lines: WHLHA correlations. Two-headed arrows: Induced correspondences (full—thermal; dashed—photochemical).

increases with the number of nodal surfaces, *etc.*... Two specific points should be noted:

1) ψ_- and ψ_+^*, which would have the same energy in a square-planar molecule, are split as shown to become the HOMO and LUMO, respectively.

2) As must often be done when the "product" is made up from two separate molecules, it is thought of as representing a point along the reaction coordinate at which they are still close enough to interact. Otherwise, all four combinations of the bonding π-orbitals would be degenerate, and there would be no justification for characterizing π^{*z}_-, the most bonding combination of the π* orbitals, as the LUMO and ignoring the other three.

When the usual WHLHA correlation lines are drawn into Figure 4, the reaction is found to be both thermally and photochemically forbidden, because the strongly bonding doubly-occupied orbital σ-(AS) correlates with the LUMO, which is unoccupied in the ground-state and only singly-occupied in the lowest excited state.

Adopting those features of OCAMS which have already been introduced, we can regard the WHLHA correlation lines as direct correspondences and investigate whether the missing correspondence can be induced by a distortion that might serve as a reasonable reaction coordinate. In the ground state reaction this is: $\sigma_-(AS) \leftrightarrow \pi^z_+(SA)$, which can be induced by distortion along an AA symmetry coordinate. In the excited state reaction, the singly-occupied HOMOs and LUMOs correspond directly with one another, so the required correspondence is: $\sigma_-(AS) \leftrightarrow \pi^y_-(SA)$, which also requires a distortion of type AA. The observed photochemical fragmentation can thus be rationalized on the basis of a reaction coordinate that is antisymmetric to both m_1 and m_2; but then, why is thermal fragmentation, which seems to require the same type of reaction coordinate, not observed too?[28]

The reason for the apparent discrepancy is that two coordinates—or two orbitals for that matter—can both be characterized as AA and still not be symmetrically equivalent, because their characterization on the basis of m_1 and m_2, alone is inadequate in the higher symmetry adopted for the system[29].

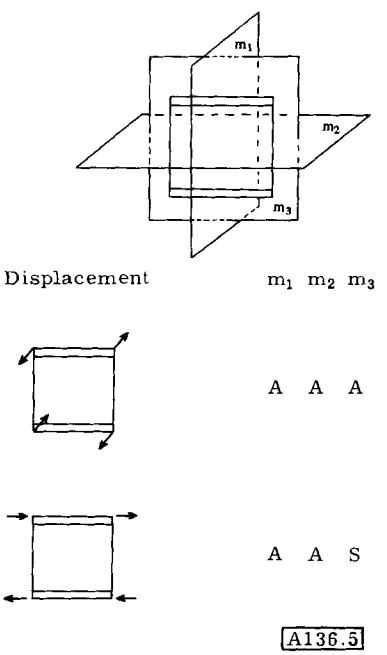
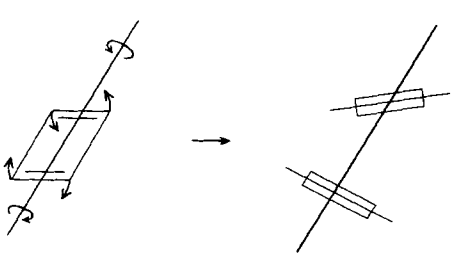


Fig. 5. AA coordinates of cyclobutadiene.

Of the two AA coordinates in Figure 5, one is an "out-of-plane twist" that is antisymmetric with respect to the discarded symmetry element m_3 and the other is an "in-plane glide", symmetric to m_3. The former, which is fully characterized as AAA, might serve as a reasonable reaction coordinate for concerted rupture of both σ bonds to yield two acetylene molecules, as in Scheme 2; the latter, AAS, coordinate would not, since weakening of the bonds initially on the sides of the rectangle would presumably be accompanied by bonding across the diagonal to form a transoid four-carbon chain.

Scheme 2.



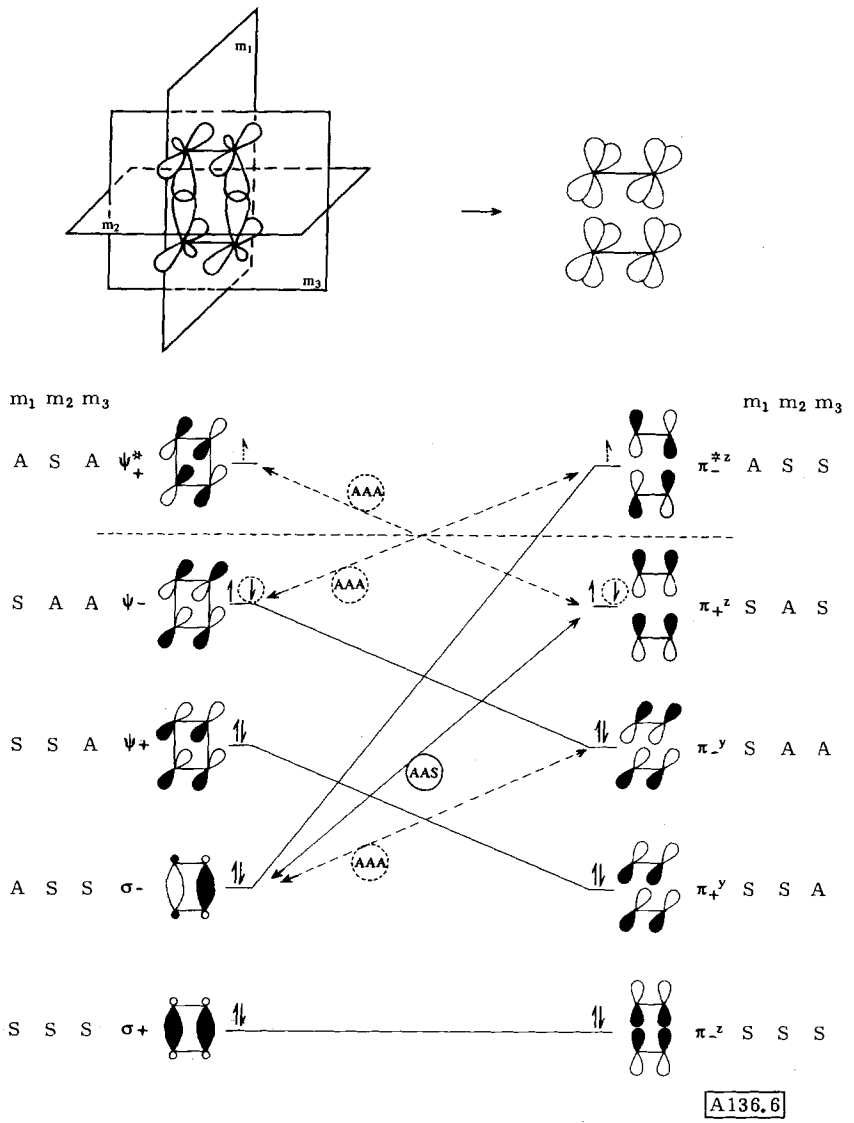


Fig. 6. Correspondence diagram for fragmentation of cyclobutadiene (higher unoccupied orbitals not shown).

In order to determine which of these two coordinates to associate with the thermal and which with the photochemical fragmentation, Figure 4 is redrawn as Figure 6, in which the orbitals are characterized with respect to m_1, m_2, and m_3.

The direct correspondences between the three pairs of bonding orbitals remain as before. The correspondence that has to be induced in order to allow thermal fragmentation is now seen to be of the unsuitable AAS type, and—since a reaction that is formally "allowed" by a coordinate that is geometrically unsuited to serve as a reaction coordinate is as surely prevented from taking place as one that is formally "forbidden"—failure to observe it is understandable. The $\sigma_-(ASS) \leftrightarrow \pi^y_-(SAA)$ correspondence needed to allow photochemical fragmentation is just the type shown in Scheme 2 to be appropriate. The same AAA coordinate is also capable of inducing a cross-correspondence between HOMO and LUMO, which are no longer in direct correspondence, as Figure 4 erroneously had them. The observed fragmentation behavior has thus been rationalized, but only after carrying out the analysis in *maximum symmetry*.

3.2. Dimerization of Cyclobutadiene: Alternative Product Stereochemistry

The choice of the geometry in which the analysis is carried out is not crucial; a poor choice is corrected by OCAMS by suggesting a reorientation to another geometry. The axial, noncoplanar, orientation at the top of Figure 7 was chosen for the analysis of cyclobutadiene dimerization in order to illustrate three points:

a) Maximum symmetry does not imply the imposition on the system of as many symmetry elements as possible. In the geometry adopted, the system is evidently less symmetrical than in the plane-rectangular orientation (cf. Fig. 8a) which—in addition to the three rotational axes—also has three mirror planes and a center of inversion. Figure 8a implies a product with a planar cyclobutane ring whereas Figure 7 suggests that the central ring is puckered. The two are interconvertible by means of a slight, energetically inexpensive, twist about the longitudinal axis[30], so it is fully to be expected that analyses in both geometries would yield the same result—as indeed they do. The T-orientation shown in Figure 8b has

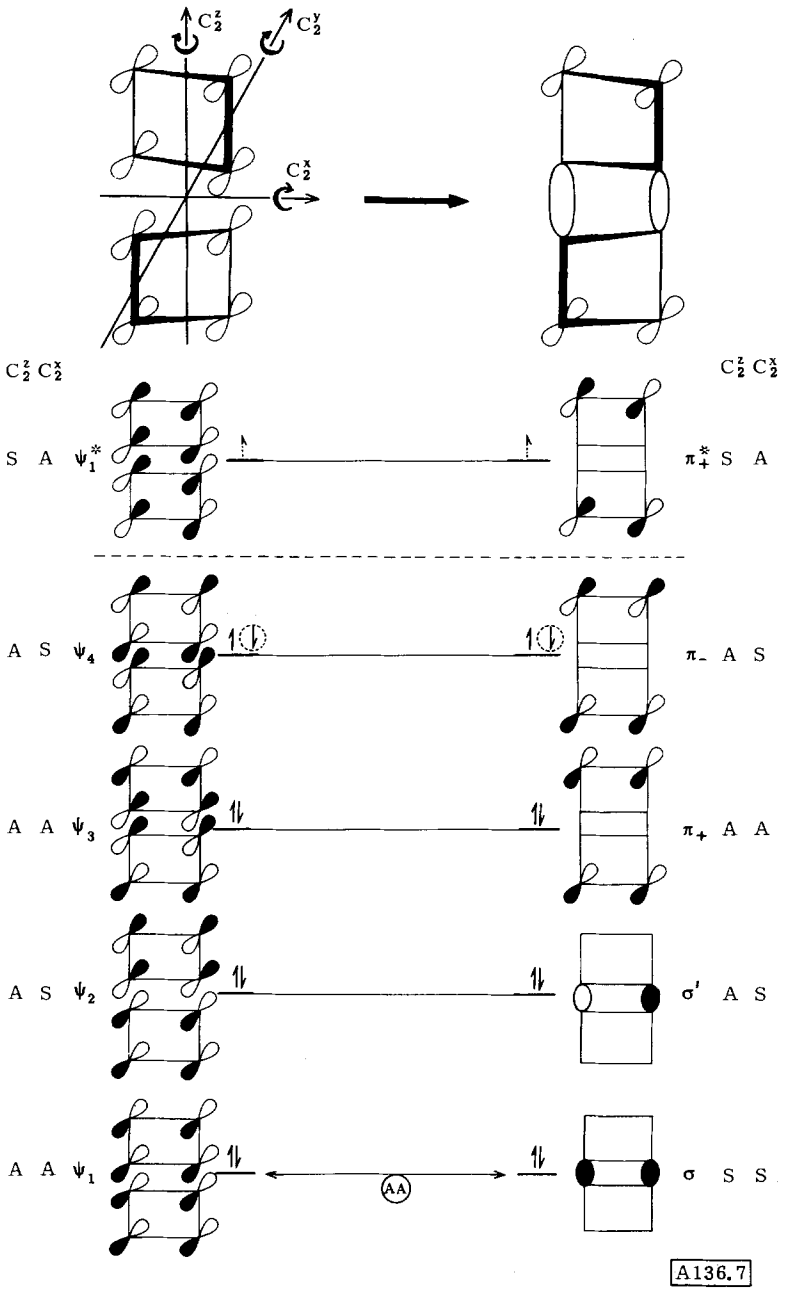


Fig. 7. Correspondence diagram for dimerization of cyclobutadiene (higher unoccupied orbitals not shown).

as many symmetry elements as the axial orientation, but it is inherently less symmetrical in that the upper molecule can use either of its two π-bonds for σ-bonding to the lower molecule, whereas the latter is constrained to bond *via* the two carbon atoms nearest to its partner. Such orientations can lead to erroneous conclusions and are avoided.

b) Rotational axes alone suffice to characterize orbitals and coordinates, mirror planes offering no particular advantages over them.

c) The analysis can be carried out in an assumed geometry which cannot possibly be that of a stable product. The axially symmetric dimer shown at the upper right of Figure 7 is too strained to be a real molecule, nor does it stand for one. What it does represent is a point along the reaction pathway at which the reactants have come close enough for σ bonding between them to begin, but beyond which increasing steric strain forces the system into either the *syn* or *anti*

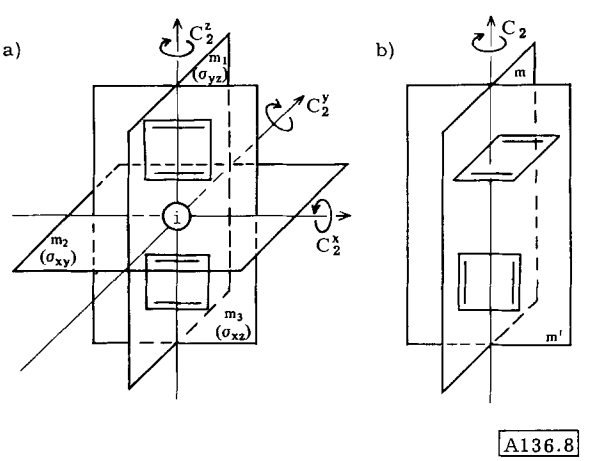


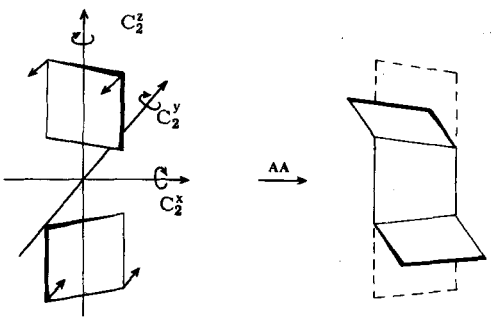
Fig. 8. Alternative initial orientations: a) Plane rectangular (acceptable); b) T-orientation (unacceptable—see text).

conformation. Which of the two stereoisomeric products will be preferred is ascertained with the aid of the correspondence diagram.

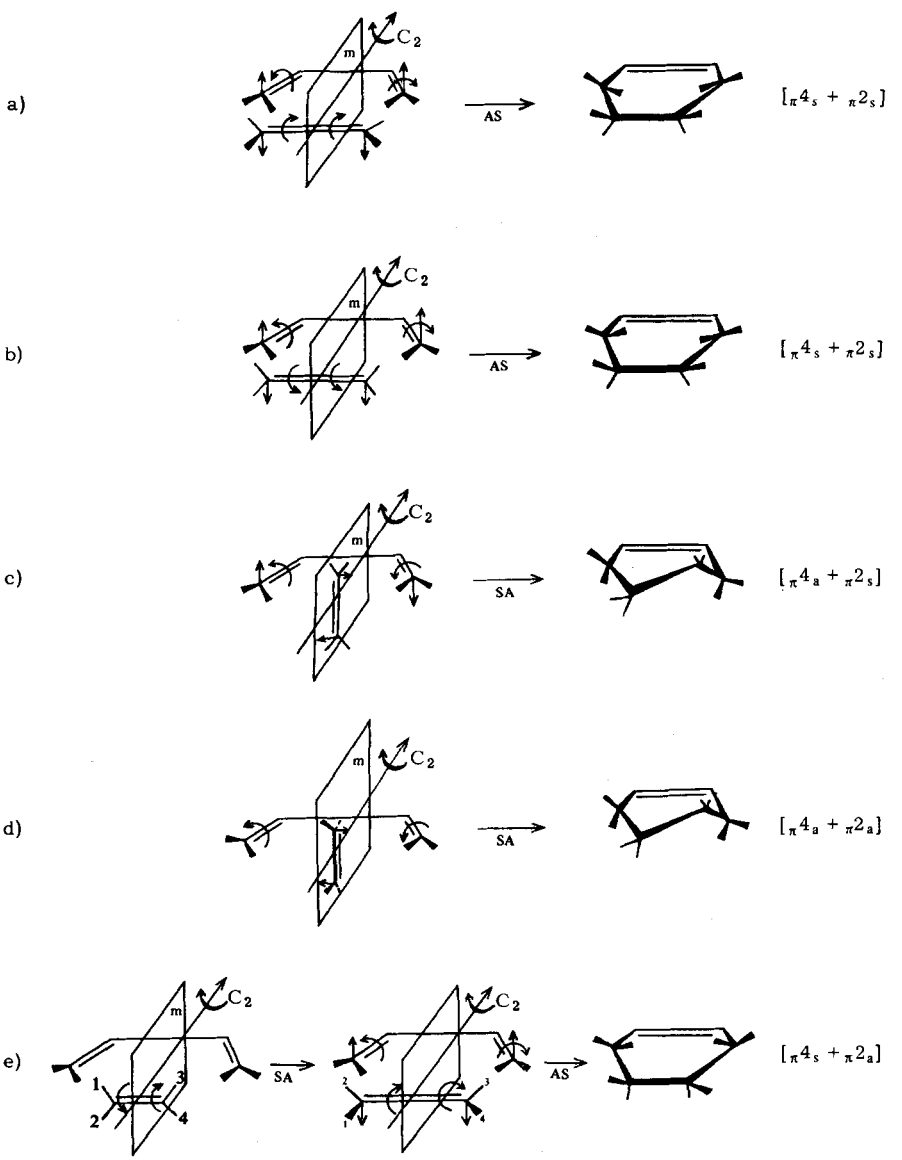
Like the products of fragmentation in Figure 6, the reactant molecules are brought close enough to interact. Provided that the twist of the two reactants about the z-axis is not too great, the ordering of the orbitals—which allows us to ignore all of the antibonding orbitals above the LUMO—is self-evident[31]. As in C_{2v}, two of the three diagnostic symmetry elements suffice to characterize the molecular orbitals fully. The choice of C_2^x and C_2^z, rather than of either one of them and C_2^y, is arbitrary.

The three uppermost pairs of doubly-occupied orbitals are in direct correspondence, so the ground-state reaction is allowed by motion along an AA coordinate (*i.e.* antisymmetric to C_2^x and C_2^z and thus necessarily symmetric to C_2^y), which induces the remaining correspondence $\psi_1(AA) \leftrightarrow \sigma(SS)$. The folding motion leading to the *syn*-dimer, shown in Scheme 3, evidently has the proper symmetry; the alternative folding motion towards the *anti* conformation is easily seen to have unsuitable AS symmetry. We might also note that the stereochemical requirements of the thermal and photochemical reactions are the same, and that photochemical fragmentation of the *syn*-dimer to cyclobutadiene would be expected to occur whereas that of the *anti*-dimer would not.

Scheme 3.



Woodward and *Hoffmann*[2] characterize the formation of either dimer as thermally allowed by virtue of the reaction



A136.9

Fig. 9. Possible pathways for $[\pi 4 + \pi 2]$ cycloaddition.

being a $[\pi 4_s + \pi 2_a]$ cycloaddition, but favor the *syn*-isomer on the basis of secondary orbital interactions. To OCAMS, the reaction cannot uniquely be characterized as $[\pi 4_s + \pi 2_s]$ any more than $[\pi 4_s + \pi 4_s]$ or $[\pi 2_s + \pi 2_s]$, and the preference for the observed *syn*-isomer emerges from it as unambiguously primary.

4. Symmetry, Geometry, and Energy: $[\pi 4 + \pi 2]$ Cycloaddition

Although the predictions of OCAMS with regard to the prototype Diels-Alder reaction, cycloaddition of ethylene to butadiene, do not differ essentially from those of WHLHA, this familiar reaction serves as a good vehicle for conveying several additional features of the method:

a) How the choice of an orientation of reactants and products in which to carry out the analysis affects the results of that analysis.

b) How the method can be applied to systems in which the product is inherently less symmetrical than the reactant, because it may be formed as one of several chemically identical isomers, differing only in the bonding sequence of indistinguishable atoms.

c) How a possible reaction path that is not a symmetry coordinate can be investigated.

d) How far symmetry alone can take us, and when considerations of energy—always implicit in orbital symmetry arguments—must be made explicit.

Woodward and *Hoffmann*[2] characterize ground-state cycloaddition as "allowed" when both reactants react suprafacially $[\pi 4_s + \pi 2_s]$ or antarafacially $[\pi 4_a + \pi 2_a]$ and the excited state reaction as allowed when either—but not both—of the reaction partners reacts antarafacially, *i.e.* $[\pi 4_s + \pi 2_a]$ or $[\pi 4_a + \pi 2_s]$.

The coplanar orientation of the reactants, shown in Figure 9a, emphasizes the analogy with a six-membered aromatic ring, and seems to be a good starting point for the allowed $[\pi 4_s + \pi 2_s]$ reaction, but it is certainly not the only one. For example, in Figure 9b, the ethylene molecule has been rotated about its axis so that each of its methylene groups is bisected by the plane containing the butadiene skeleton; this is an equally good initial orientation for $[\pi 4_s + \pi 2_s]$ cycloaddition proceeding along an AS coordinate. Beginning with the orientation in 9c, a geometry suitable for $[\pi 4_a + \pi 2_s]$ cycloaddition is obtained by motion along the SA coordinate pictured. The initial mutual disposition of reactants shown in 9d would seem to be an eminently suitable one from which to begin along the SA pathway leading to $[\pi 4_a + \pi 2_a]$ cycloaddition. The fourth mode of cycloaddition, $[\pi 4_s + \pi 2_a]$, does not suggest an initial geometry from which the reaction can proceed along a single symmetry coordinate. A suitable reaction coordinate can, however, be put together out of a sequence of two: Beginning from the same initial orientation as in 9b, 9e proceeds *via* a conrotatory twist of the ethylenic CH_2 groups by 90° and generates a coplanar orientation which differs from that of 9a only in that the H-atoms—say 1 and 3—that were initially *cis* to one other have become *trans*. When this is followed by the same AS coordinate as in 9a, *cis*-geometry is obtained once more, but the ethylene has reacted antarafacially.

Clearly, whereas some initial orientations appear to be particularly well suited to a single pathway, others can serve as good starting points for more than one, and some pathways—

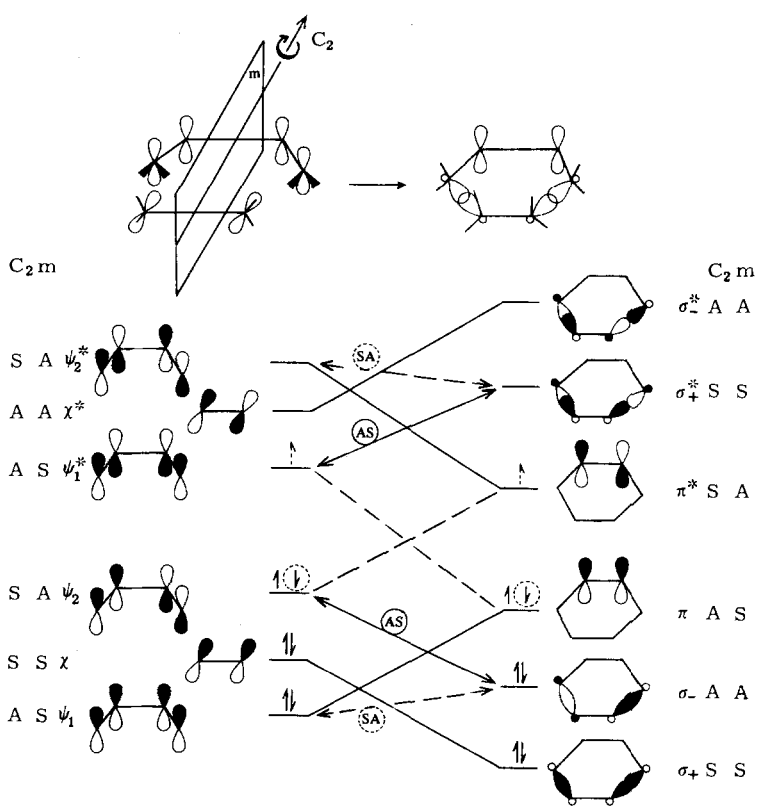


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Fig. 10. Correspondence diagram for $[\pi 4 + \pi 2]$ cycloaddition (initial geometry of Fig. 9b).

notably that for $[\pi 4_s + \pi 2_a]$ cycloaddition—do not seem to have a good starting point at all. A good method of analyzing reaction pathways by symmetry should not be dependent on the way the problem has been set up. We will find that OCAMS is substantially independent of the geometrical model employed, but not entirely: A poor choice of an assumed initial orientation of reactants may obscure a possible pathway; it will not, however, let a "forbidden" pathway appear to be "allowed".

4.1. The Choice of an Initial Geometry

Rather than begin with the too-familiar orientation a of Figure 9 with its intimations of aromaticity, we base the correspondence diagram, Figure 10, on that of b. The "product" is also drawn as if it had C_{2v} geometry, although it will certainly be forced out of planarity and go into either a *cis*- or a *trans*-conformation. As in cyclobutadiene dimerization (Section 3.2), it represents a point along the reaction coordinate just before the way in which symmetry is to be broken has been chosen by the reacting system.

In the thermal reaction there are two direct correspondences: $\psi_1(AS) \leftrightarrow \pi(AS)$ and $\chi(SS) \leftrightarrow \sigma_+(SS)$, whereas the third $\psi_2(SA) \leftrightarrow \sigma_-(AA)$ is induced by an AS motion. A coordinate that is appropriately symmetric to m and antisymmetric to C_2 is that shown in Figure 9b, which is—except for the disrotation at the terminal carbons of the diene—merely a reorientation that costs no energy. The $[\pi 4_s + \pi 2_s]$ reaction is thus judged to be eminently allowed. The $[\pi 4_a + \pi 2_a]$ reaction, in contrast, does not emerge from the analysis at all.

Going on to the photochemical reaction, we see that the HOMO-LUMO cross-correspondence is direct and thus imposes no stereochemical requirements. Of the two-electron correspondences, $\chi(SS) \leftrightarrow \sigma_+(SS)$ remains, but now $\psi_1(AS)$ must be brought into correspondence with $\sigma_-(AA)$ by means of an SA displacement very similar to that in Figure 9c and also leading to $[\pi 4_a + \pi 2_s]$ cycloaddition. Now it is $[\pi 4_s + \pi 2_a]$ cycloaddition, which has the advantage of leading to a more stable *cis*-joined product that does not appear.

We try again, starting with the coplanar arrangement of Figure 9a and construct the new correspondence diagram shown in Figure 11. The two π-systems interact and, as a result, the "reactant's" π-orbitals now display marked similarity to those of a distorted benzene ring, but the orbital order is unchanged. The correspondences look different from those of Figure 10, but the conclusions are not; they are merely more complete. In the thermal reaction, there is only one direct correspondence: $\chi(AS) \leftrightarrow \pi(AS)$. The two remaining correspondences can be induced in one of two ways: 1) An AS coordinate, such as that of Figure 9a leading to $[\pi 4_s + \pi 2_s]$

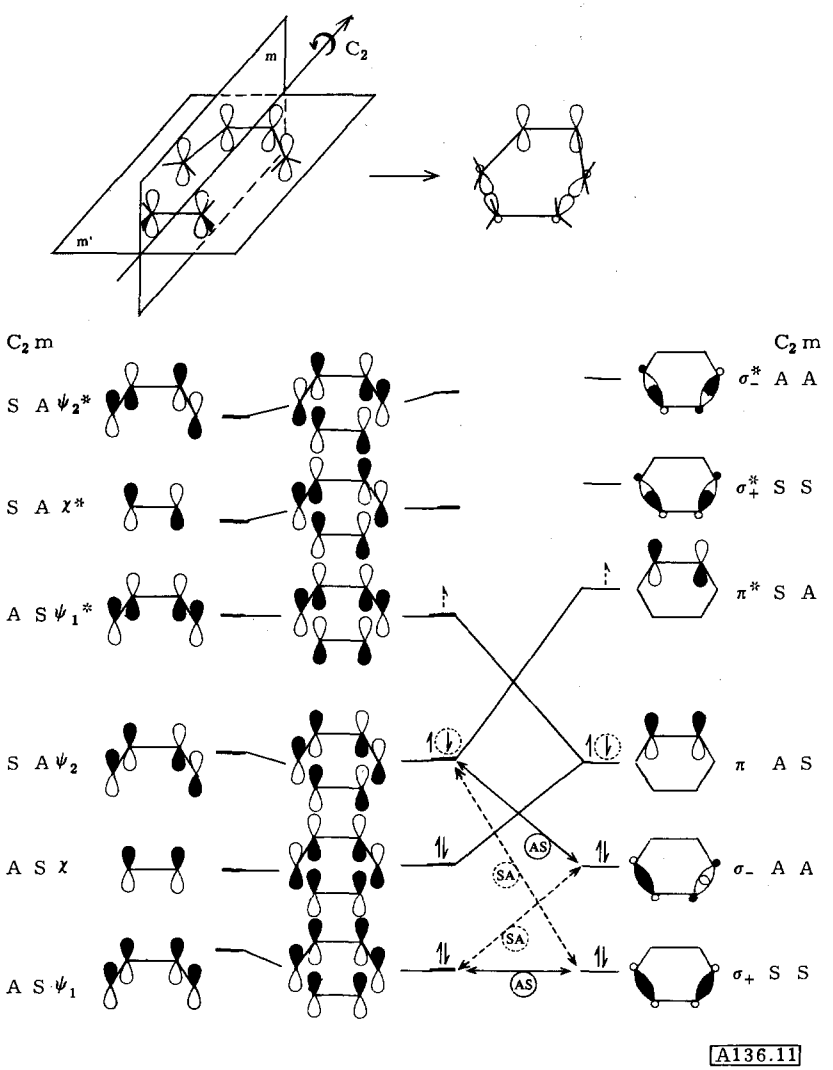


Fig. 11. Correspondence diagram for $[\pi 4 + \pi 2]$ cycloaddition (initial geometry of Fig. 9a).

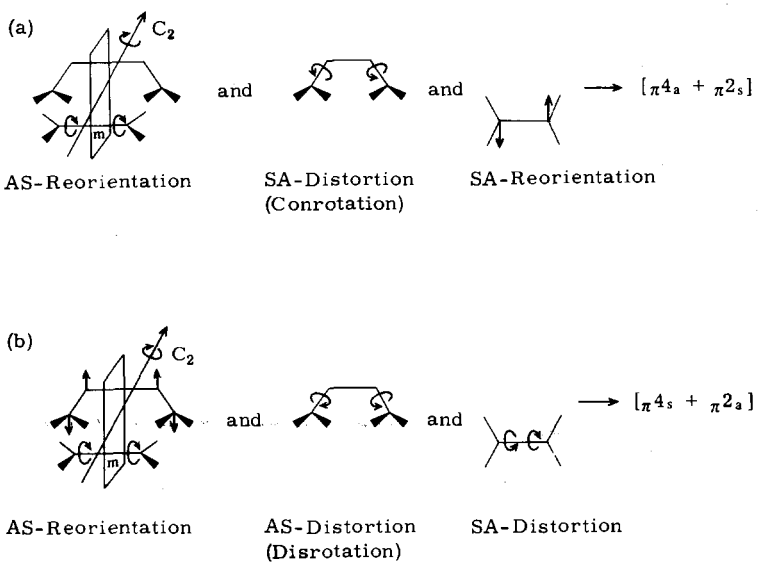
cycloaddition, induces $\psi_1(AS) \leftrightarrow \sigma_+(SS)$ and $\psi_2(SA) \leftrightarrow \sigma_-(AA)$; 2) Motion along an SA coordinate induces: $\psi_1(AS) \leftrightarrow \sigma_-(AA)$ and $\psi_2(SA) \leftrightarrow \sigma_+(SS)$. We now note that a rotation of the ethylene molecule about the C_2 axis, which is SA in character, generates the initial orientation of Figure 9d and thus leads to $[\pi 4_a + \pi 2_a]$ cycloaddition. The reorientation costs no energy; the conrotatory distortion in 9d is no more severe than that in 9c. Thus, apart from the inherent instability of the *trans*-joined product, $[\pi 4_a + \pi 2_a]$ cycloaddition is allowed.

Why then does this mode of reaction not emerge from Figure 10? It is not the "aromaticity" of the coplanar orientation assumed in Figure 11 that makes it a better choice; the π-interaction does not change the orbital sequence and so—for qualitative purposes—it is irrelevant. The advantage of the coplanar orientation is simply that it can be brought into a suitable geometry for either $[\pi 4_s + \pi 2_s]$ or $[\pi 4_a + \pi 2_a]$ cycloaddition by motion along a single symmetry coordinate, AS or SA respectively. The initial disposition of reactants in Figure 9b is ideal for $[\pi 4_s + \pi 2_s]$ but it is too remote from that required for $[\pi 4_a + \pi 2_a]$. In order to convert the initial geometry of Figure 9b to that of Figure 9d, motion must occur along two symmetry coordinates in which only the ethylene molecule is rotated: (1) About its longitudinal axis (AS) to the initial orientation of a; (2) about the C_2 axis (SA). Another possible sequence is: (1') about the C_2 axis to the orientation in c; (2') about its "new" longitudinal axis (AA). Neither of these reorientation sequences costs any energy, but both formally destroy the symmetry of the system completely before restoring it, so the prediction of Figure 11, that thermal $[\pi 4_a + \pi 2_a]$ cycloaddition is allowed, is not made by Figure 10.

Another paradox concerns the photochemical $[\pi 4_a + \pi 2_s]$ reaction, that does not appear in Figure 11, even though it is allowed by Figure 10. In both, the HOMO-LUMO correspondences are direct, but in Figure 11 the two lowest reactant orbitals are AS orbitals whereas in the product one is AA and the other is SS. As a result, a proper reaction coordinate for photochemical cycloaddition would involve motion along both an AS and a SA coordinate. When it is realized that the initial orientation of Figure 9a is converted by rotation of ethylene about its axis (AS) to that of Figure 9b, from which—as confirmed by Figure 10—a rotation about the C_2 axis (SA) leads to $[\pi 4_a + \pi 2_s]$ cycloaddition, the paradox is resolved.

We have seen some of the limitations of symmetry arguments when these are divorced from consideration of energy, particularly when either the reactant or product is a pair of molecules that can be arbitrarily oriented relative to one another. Characterizing motions in terms of their symmetry properties alone cannot distinguish reorientations, which cost no energy, from molecular distortions, which do. Thus the sequence just described, in which an AS reorientation followed by an SA reaction coordinate that includes a rather mild distortion, is equivalent—purely in terms of symmetry—to the composite motion of Figure 9e. It is obvious from the dissection of these two composite motions in Scheme 4 that they are energetically very different: It is the fact that two of the symmetry coordinates in (a) are reorientations whereas two of (b) are distortions—one quite severe—that makes photochemical $[\pi 4_a + \pi 2_s]$ cycloaddition different from the $[\pi 4_s + \pi 2_a]$ mode. Therefore, though the former leads to a less stable product, it can be regarded as genuinely "allowed", whereas the latter cannot[32].

Scheme 4.



4.2. Alternate Bonding Patterns

An important property of $[\pi 4_a + \pi 2_s]$ and $[\pi 4_a + \pi 2_a]$ cycloadditions, which they share with many other reactions, is illustrated in Figure 12. At the top left and right of the figure are the respective initial orientations of Figure 9c and 9d, which are interconvertible by means of a rotation of ethylene about its longitudinal axis (AA). The reactant pair has C_{2v} symmetry in both orientations and the molecular orbitals are characterized accordingly.

The product, as represented at the top center of Figure 12, is less symmetric, since it can be formed in either of two bonding sequences: [1ul4] or [1lu4], depending on whether the upper carbon atom of ethylene bonds to C_1 and the lower to C_4, or *vice versa*. As in previous examples, we can define the "product" to represent a point along the

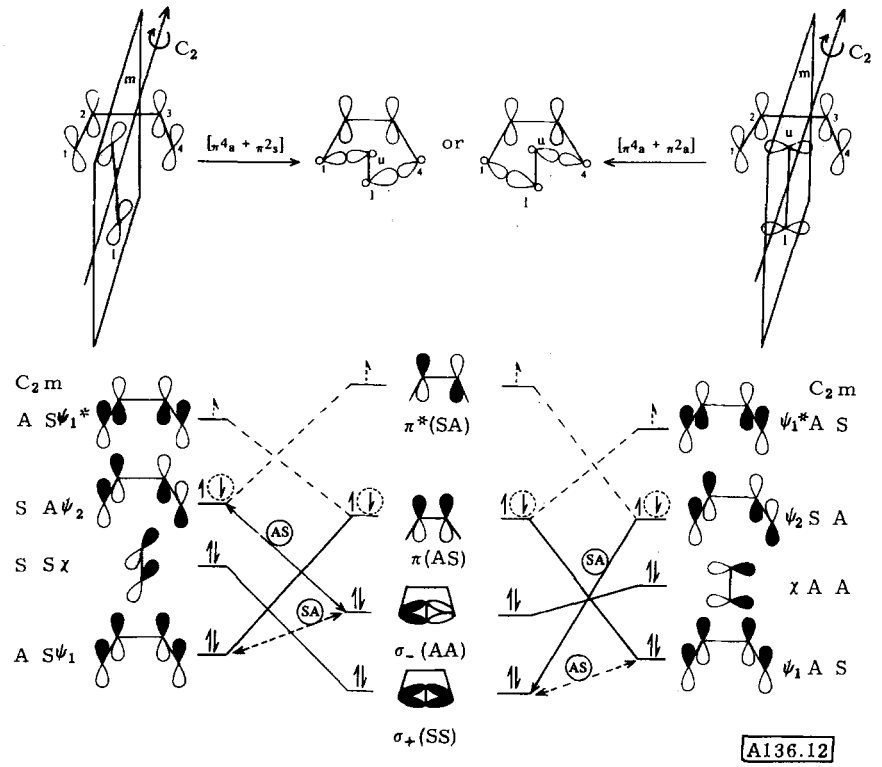


Fig. 12. Correspondence diagrams for $[\pi 4_a + \pi 2_s]$ and $[\pi 4_a + \pi 2_a]$ cycloaddition (higher unoccupied orbitals not shown).

reaction coordinate just before symmetry is reduced below that of the reactants. Now, however, the fact that two bonding schemes—not just two possible geometries—can be generated, must be reflected in the symmetry properties of the product's molecular orbitals.

The HOMO, π, and the LUMO, π^*, pose no problem; they are the same in both enantiomers. Neither do the two lowest orbitals of either product. In [1ul4], they are the symmetric and antisymmetric combinations of the 1—u and 4—l σ bonds; in [1lu4] they are the analogous linear combinations of 1—l and 4—u. In order to restore C_{2v} symmetry to the product, it is generalized to include both alternatives, so that the lowest orbital is represented by a suitable superposition of the two symmetric combinations and the second by a superposition of the antisymmetric ones. The question that arises is how to specify correctly the phase of each superposition. Specifically, should the lowest orbital be SS as in the figure, or should it be the *a priori* equally valid SA orbital, in which 4—l and 1—u are of opposite phase to 1—l and 4—u? The decision is dictated by the requirement that the generalized orbital be consistent with an equal probability of forming either enantiomer. Since C_1, for example, must be equally bonding with C_u and C_l a moment before the course of the reaction has been chosen, 1—u and 1—l must have the same phase. This condition suffices to fix $\sigma_+(SS)$ and $\sigma_-(AA)$ as the two σ-orbitals of the generalized product.

The correspondence lines are drawn in the usual way. Thermal $[\pi 4_a + \pi 2_s]$ cycloaddition formally requires that the $\psi_2(SA) \leftrightarrow \sigma_-(AA)$ correspondence be induced by an AS displacement, but geometry requires an SA motion, as is evident from Figure 9c. The latter does have the proper symmetry to induce the $\psi_1(AS) \leftrightarrow \sigma_-(AA)$ correspondence required for photochemical $[\pi 4_a + \pi 2_s]$ cycloaddition, which is therefore allowed. Conversely it is the thermal $[\pi 4_a + \pi 2_a]$ cycloaddition which is allowed under the geometrically appropriate SA displacement shown in Figure 9d, whereas the photochemical reaction calls for an unsuitable AS motion. Our previous conclusions have thus been reinforced. The correspondence diagrams in Figure 12 are different from those of Figures 10 and 11, but the conclusions from them are all mutually consistent and the additional bits of insight supplied by each of them complement one another.

5. Open Shell Reactions

The three topics taken up in this section are related by the fact that unpaired electrons enter into all of them:

1) Odd-electron systems lend themselves as easily to OCAMS as do those with an even number of electrons, though their photochemical reactions introduce a new ambiguity.

2) The distinction between the photochemical reactions of singlet and triplet excited states goes beyond any qualitative molecular orbital theory, which necessarily neglects electron correlation, but does call for some comment in the present context.

3) Several reactions in which the product has a different spin-multiplicity from that of the reactant have been reported, and will presumably become more common. An orbital method like OCAMS cannot deal with such reactions without modification, but a suggestion can be made as to the direction which a possibly fruitful extension of the present approach might take.

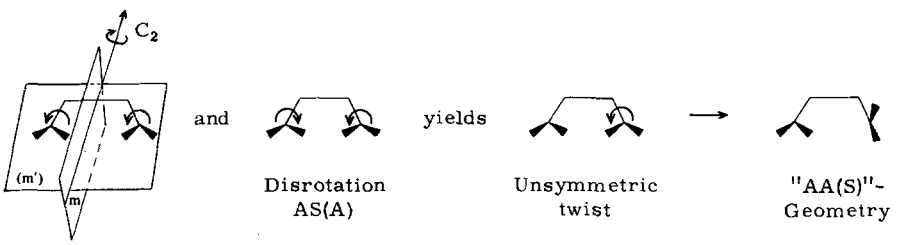
5.1. Odd Electron Reactions: Cyclization of Butadiene Anion

When an electron is added to *s-cis*-butadiene, it occupies the LUMO, ψ_2^*, of Figure 2, which becomes a correspondence diagram for the thermal cyclization of the radical anion, pro-

vided the five arrows are taken to represent five electrons, rather than four in two alternative configurations.

As in the thermal cyclization of the neutral diene, correspondence between ψ_1(AS) and π(AS) is direct, and the remaining two-electron correspondence, ψ_2(SA)$\leftrightarrow\sigma$(SS) calls for a conrotation. The one-electron correspondence $\psi\dagger$(AS)$\leftrightarrow\pi^*$(SA) requires an AA displacement, which can be seen in Figure 3 to describe neither a conrotation nor a disrotation, but an in-plane distortion. It is, however, shown in Scheme 5 that a 45° disrotation following a 45° conrotation generates a 90° twist of a single methylene group to a geometry that—if only momentarily—is symmetric to m' but not to C_2 or m. Scheme 5 expresses schematically the fact that—in a limited way—a superposition of an AS and an SA motion is the equivalent of an AA motion[33].

Scheme 5.



Consequently, our prediction from Figure 2 would be that the two-electron correspondences require thermal cyclization of the butadiene radical anion to be fundamentally conrotatory, but that, in order to induce the one-electron correspondence as well, some disrotation must be admixed into the conrotation, *i.e.* the two methylene groups would be expected to rotate at somewhat different rates[34].

Figure 2 can also be used to discuss the photochemical reaction. The identity of the first excited state of the product is irrelevant, since there is no apparent reason for the excited reactant not to correlate smoothly with the ground state of the product. In the excited state of the diene anion $\psi\ddagger$(SA), rather than $\psi\dagger$(AS), is singly occupied, and its correspondence to π^*(SA) is direct, so the conrotatory excited state reaction is allowed. The reverse photochemical reaction is also allowed under a conrotation, if we assume the excitation in the cyclobutene anion to be $\pi^*\rightarrow\sigma^*$, because the σ^*(AA)$\leftrightarrow\psi\dagger$(AS) correspondence, like that between σ(SS) and ψ_2(SA) requires a conrotation. If the lowest excited state were formed by a $\pi\rightarrow\pi^*$ excitation instead, the π^*(SA)$\leftrightarrow\psi_2$(SA) and π(AS)$\leftrightarrow\psi\dagger$(AS) correspondences would be direct, but that between σ(SS) and ψ_1(AS) would call for a disrotatory, AS-type, displacement. Thus, as will always be the case in photochemical reactions, a reliable prediction cannot be made unless the reactive excited state is known, though—as has been noted—a firm characterization of the lowest excited state of the product can be dispensed with when there is only one unpaired electron in the system.

5.2. Comments on Photochemical Reactions

The applicability of orbital symmetry arguments to photochemical reactions, a question which has generated extensive discussion[35], will only be touched upon briefly here.

In the preceding example it was noted that, in contrast to thermal reactions, where it is sufficient to know which orbitals are occupied and which are vacant, a reliable OCAMS treatment of a photochemical reaction requires—at the very least—identification of the HOMO and LUMO of the reactant. When the reactant has only one unpaired electron, this is also a sufficient condition, but in photochemical reactions of even-electron systems it is not. *Van der Lugt* and *Oosterhoff* early raised the question whether a reactant excited by a two-electron excitation to a state in which both were in the LUMO would not "funnel through" to the ground-state, in much the same way as has been postulated above for odd-electron systems, so rapidly that the first excited singlet ($HOMO^1$ $LUMO^1$) is bypassed entirely[36]. Even when the first excited singlet is formed, internal-conversion to a vibrationally excited ground-state molecule must be considered. The product will then be formed in its ground-state whenever, before the reactant is vibrationally deactivated, vibrational energy can find its way into a coordinate of proper symmetry—and geometry—to induce the necessary correspondence to the ground state of the product. Internal conversion is ordinarily such a facile process—except perhaps for very small molecules in the dilute gas phase—that is seems reasonable to doubt whether configuration correlation between the lowest excited singlet states of reactant and product can be a reliable qualitative criterion for the prediction of photochemical pathways.

It is with this reservation in mind that all of the correspondence diagrams in this report have been drawn so as to suggest that the photochemical reaction occurs between the lowest triplets of the reactant and product. These are sufficiently long-lived with respect to intersystem crossing to the reactant ground-state for an "allowed" open-shell reaction to be considered a generally accessible pathway connecting them. To be sure, a reaction in which the lowest triplet of the reactant crosses over smoothly to the ground-state singlet of the product can be envisaged. Such a process would be analogous to the thermal singlet-triplet reactions to be discussed briefly in the following subsection, and would similarly occur only in special circumstances. Ordinarily, the triplet state of the reactant would presumably either decay to its own singlet ground-state, in which case the reaction would not occur, or maintain its multiplicity until the triplet product has been produced, and can decay at leisure to its own ground-state.

5.3. Singlet-Triplet Reactions: Isomerization of Dewar-Benzene

Several reactions have recently been described in which a relatively unstable reactant in its singlet ground-state either

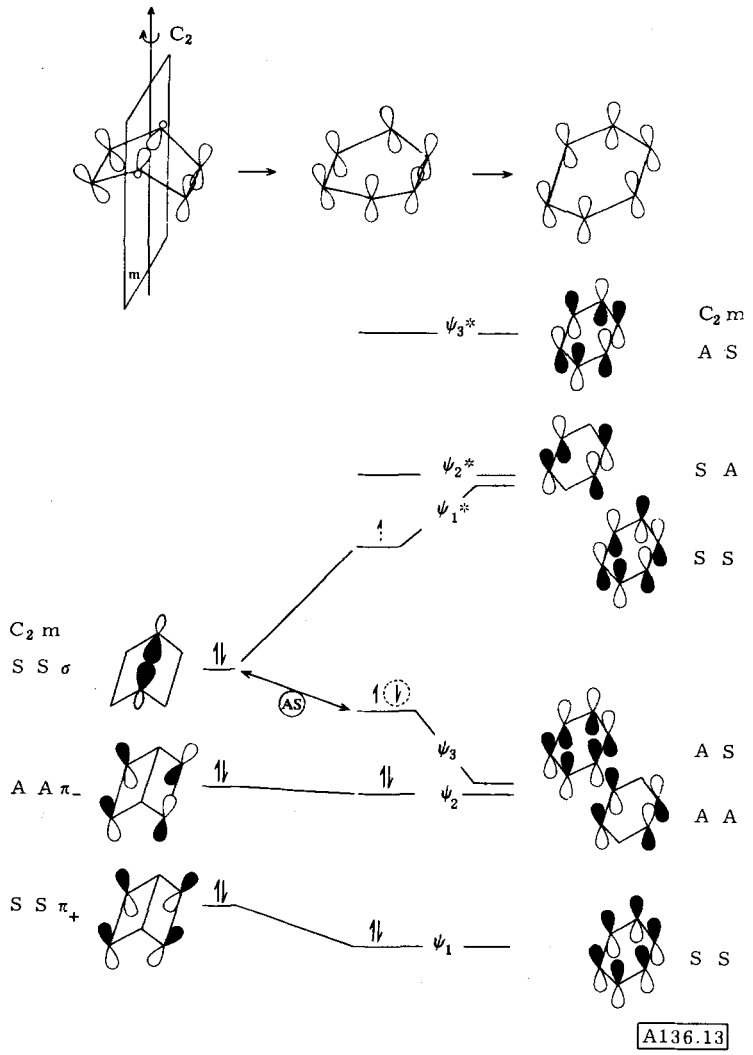


Fig. 13. Correspondence diagram for Dewar-benzene—benzene isomerization (higher unoccupied orbitals of reactant not shown).

decomposes to a singlet and a triplet fragment or isomerizes to the triplet of its more stable isomer[37].

The correspondence diagram for the interconversion of Dewar-benzene and benzene shown in Figure 13 includes only the three occupied orbitals of the reactant. The familiar six molecular orbitals of benzene, which include two degenerate pairs, are shown at the extreme right. The simplest way of bringing reactant and product to a common symmetry, in this example C_{2v}, is to work backwards and distort the product slightly in the direction of the reactant, *i.e.* to bend two *para*-disposed carbon atoms out of the molecular plane towards one another. As a result, the two degeneracies are split as shown, ψ_3(AS) going up in energy and ψ_1^*(SS) going down.

In the thermal reaction, the one correspondence that is not direct is σ(SS)$\leftrightarrow\psi_3$(AS), which requires distortion of the Dewar-benzene molecule along a coordinate that is antisymmetric with respect to C_2 but symmetric with respect to m. If one of the σ-bonded carbon atoms were pulled outward along an AS coordinate, such as that shown at the top of Figure 14, the other atom would move in the same direction and the long bond would not be ruptured. Such a motion is clearly inappropriate for generating ground-state benzene, so thermal isomerization is forbidden.

The total energy of Dewar-benzene is not only higher than that of ground-state benzene, but is above that of its lowest triplet as well. Its conversion to the latter can occur if two conditions are fulfilled simultaneously:

1) A mechanism is provided for uncoupling the antiparallel spins of an electron pair in one doubly-occupied orbital, prefer-

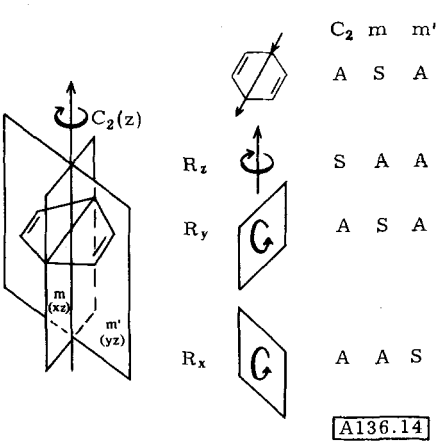


Fig. 14. Geometrically inappropriate AS-coordinate and the three rotational coordinates of Dewar-benzene.

entially that in σ(SS), which is not in direct correspondence with a doubly-occupied orbital of the product;

2) one of these electrons can then pass directly over to $\psi_3^\dagger$(SS), but an AS perturbation must still be found that will allow the other electron to pass from σ(SS) to ψ_3(AS).

A mechanism with the correct properties to fulfil both requirements at once is spin-orbit coupling. The three components of spin of a triplet have the symmetry properties of rotations about three perpendicular axes. In Figure 14 we see that rotation in the *xz*-plane, that including m, is of the proper symmetry to induce a correspondence between an SS and AS orbital. It must be stressed that we are not speaking of a molecular rotation, which—though it has the proper symmetry—does not affect the potential energy of the reacting system and is therefore ineffective. The perturbation is spin-orbit coupling which, as it uncouples the opposing spins of a pair of electrons, produces a net spin about just the right axis—*y* in our example—to generate the lowest triplet of benzene.

Although a spin-orbit coupling mechanism of this type has been shown to be theoretically sound, and to be of reasonable magnitude in at least one case[38], there is as yet neither experimental nor theoretical evidence that it is in fact operative. Moreover, since it represents at best a future modification designed to broaden the scope of OCAMS beyond its present limits, it provides an appropriate point at which to conclude this report.

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[22] We distinguish between correlation and correspondence by denoting the former by ⇔ and the latter by ↔.
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[32] A "photochemical Diels-Alder reaction" which is formally $[\pi 4_s + \pi 2_a]$ does seem to occur in the cyclization of hexatriene. In this case, however, the reaction is allowed by OCAMS because the "diene" and "dienophile" are part of the same conjugated polyene. This reaction, and also contravention of the Woodward-Hoffmann rule concerning thermal $[\pi 2_s + \pi 2_a]$ cycloaddition, are discussed at length in ref. [3].
[33] As explained in ref. [4], the composite coordinate (AS *and* SA) is equivalent *in second order* to an AA symmetry coordinate. Formally, the reducible representation $[A_2 + B_2]$ introduces second order terms of the irreducible representation: $A_2 \times B_2 = B_1$ into the potential energy.
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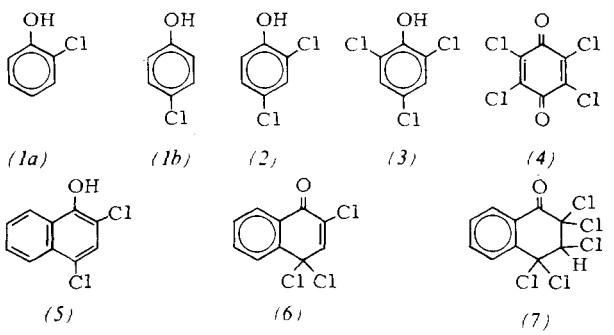
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

Nonpollutative Chlorination and Chlorinating Oxidation of Phenols[**]

By *Hans Lübbecke* and *Peter Boldt*[*]

On production of chloranil *(4)* from phenol and chlorine, hydrochloric acid is formed as a polluting by-product[1].—We have now found that *(4)* can be obtained in 94 and 88% yield respectively without by-products (except water) by treatment of phenol or hydroquinone with hydrogen peroxide/hydrochloric acid. Starting from phenol it is convenient, as in the present-day industrial process[1], to isolate *(3)* as an intermediate. Production of *(3)*, the mixture of *(1a)* and *(1b)* (*ca.* 1:1), of *(2)*, and of *(4)* (from hydroquinone) can be performed with a slight excess of hydrogen peroxide. The same applies to the reaction of α-naphthol to give *(5)*, *(6)*, and *(7)*. [*(6)* and *(7)* are intermediates for the preparation of 2-chloro- and 2,3-dichloro-1,4-naphthoquinone[2].] *(3)*, *(4)*, and *(7)* are obtained directly in pure form (conditions given in Table 1).



(1a) *(1b)* *(2)* *(3)* *(4)*

(5) *(6)* *(7)*

As illustrated by the preparation of *(3)* and *(4)* the yields can be raised or the amount of hydrogen peroxide reduced by addition of magnesium chloride.

Use of hydrogen peroxide/hydrochloric acid instead of chlorine gas also offers the advantages of easier handling and measuring when working on a laboratory scale[3].

2,4,6-Trichlorophenol (3)

30% hydrogen peroxide (40 ml, 0.4 mol) is added within 15 min to a stirred, ice-cooled mixture of phenol (9.4 g, 0.1 mol), magnesium chloride (10 g, 0.11 mol), and conc. hydrochloric acid (150 ml). Warming to 50°C for 4 h, followed by filtration and drying yielded 19.4 g (99%) of *(3)*.

Cloranil (4) from (3)

30% hydrogen peroxide (15 ml) is added dropwise within 15 min to a mixture of *(3)* (3.5 g, 18 mmol) and magnesium chloride (26 g, 0.27 mol), the temperature is then raised to 100°C and a further amount of hydrogen peroxide (25 ml, total amount 0.4 mol) added in three portions—at intervals of 6 h—and stirring continued for 32 h at 100°C. After washing with methanol and drying the filter cake yielded 4.2 g (96%) of *(4)*.—The other products were prepared in the same way as *(3)*.

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(1a), 95-57-8; *(1b)*, 106-48-9; *(2)*, 120-83-2; *(3)*, 88-06-2; *(4)*, 118-75-2; *(5)*, 2050-76-2; *(6)*, 1133-38-6; *(7)*, 2243-28-9; phenol, 108-95-2; hydroquinone, 123-31-9; α-naphthol, 90-15-3

Table 1. Reaction conditions for chlorination and chlorinating oxidation of phenol and α-naphthol with conc. HCl and 30% H_2O_2.

Reactant	[mol]	HCl [ml]	H_2O_2 [ml]	H_2O_2 [mol]	T [°C]	t [h]	$MgCl_2$ [mol]	Product	Yield [%]
Phenol	0.2	300	20	0.2	0	4	—	*(1a)* and *(1b)*	56 [b]
Phenol	0.2	300	42	0.4	0	4	—	*(2)*	47 [c]
Phenol	0.1	150	40	0.4	50	4	0.11	*(3)*	99
Phenol	0.05	75	20	0.2	50	4	—	*(3)*	83
(3)	0.018	270	40	0.4	100	50	0.27	*(4)*	96
(3)	0.018	200	70	0.7	100	50	—	*(4)*	96
Hydroquinone	0.05	400	30	0.3	95	2	0.37	*(4)*	88
α-Naphthol [a]	0.05	100	10	0.1	0	0.7	—	*(5)*	70 [d]
α-Naphthol [a]	0.05	100	15	0.15	0	1.5	—	*(6)*	73 [d]
α-Naphthol [a]	0.05	100	25	0.25	20	4	—	*(7)*	89 [d]

[a] Solution in 60 ml of glacial acetic acid. [b] Work-up according to ref. [2], p. 680. [c] Work-up according to ref. [2], p. 681. [d] Work-up according to ref. [2], p. 691.

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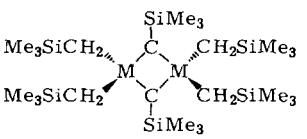
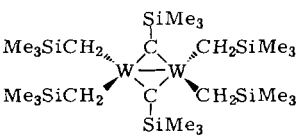
Tetrakis(trimethylsilylmethyl)bis(μ-trimethylsilylmethylidyne)ditungsten[**]

By *Richard A. Andersen, A. Lee Galyer,* and *Geoffrey Wilkinson*[*]

The first examples of bridged carbyne complexes were the compounds $(RCH_2)_2M(\mu\text{-}CR)_2M(CH_2R)_2$, M = Nb, Ta; R = $SiMe_3$, which were obtained by the interaction of MCl_5 with Me_3SiCH_2MgCl in diethyl ether/petroleum mixture[1]. Confirmation of the structure (1) proposed on the basis of NMR spectra was provided by X-ray crystallography of the niobium complex[2]. The four-membered M_2C_2 ring can be regarded as quasi-aromatic and no metal-metal bonding need be involved.



(1)



(2)

We have now synthesized a new example of this type of alkyl derivative by the interaction of tungsten(IV) chloride and $(Me_3SiCH_2)_2Mg$ in tetrahydrofuran[3]. The ^{1}H-NMR spectrum of the red-brown polycrystalline complex $(RCH_2)_2W(\mu\text{-}CR)_2W(CH_2R)_2$, R = $SiMe_3$, has resonances at τ = 9.72, 9.87, and 9.45 in area ratios 18:4:9 due to $(CH_3)_3SiCH_2W$, $(CH_3)_3SiCH_2W$, and $(CH_3)_3SiCW$ respectively. The structure *(2)* is further defined by the ^{13}C-NMR spectrum (Table 1), particularly by the strongly deshielded bridging carbyne carbon atom. The ^{13}C-NMR spectra of the niobium and tantalum analogs and also of the metal-metal bonded species[4] $(RCH_2)_3M{\equiv}M(CH_2R)_3$, M = Mo and W; R = $SiMe_3$, are also given for comparison. The diamagnetism of the tungsten compound where the metal atom is formally pentavalent as in the Nb and Ta complexes requires the presence of a W—W single bond in addition to the bridge groups.

Table 1. ^{13}C-NMR data of alkylmetal compounds [a].

	$(CH_3)_3SiCH_2$	$(CH_3)_3SiCH_2$	$(CH_3)_3SiC$
$(Me_3SiCH_2)_4W_2(CSiMe_3)_2$ [b]	2.20, 3.00	69.0	354
$(Me_3SiCH_2)_4Nb_2(CSiMe_3)_2$	3.41, 3.98	64.2	406
$(Me_3SiCH_2)_4Ta_2(CSiMe_3)_2$	3.63, 4.97	79.3	406
$(Me_3SiCH_2)_6Mo_2$	4.60	65.0	
$(Me_3SiCH_2)_6W_2$ [c]	4.70	79.6	

[a] Varian XL-100 spectrometer, 25.14 MHz, in C_6D_6, δ values (in ppm, $\delta_{C_6D_6}$ = 129 ppm).
[b] $J(^{183}W\text{-}^{13}C)$ = 74 Hz.
[c] $J(^{183}W\text{-}^{13}C)$ = 79 Hz.

The presence of alkyl and alkylidyne groups in the same molecule is supported by deuterolysis. The tungsten complex is not hydrolyzed by D_2O neat or in decalin solution but with 6 M D_2SO_4 it gives Me_4Si (76% D_1, 8.8% D_2, and 14% D_3; determined by mass spectrometry). The tantalum complex with D_2O gives Me_4Si (74% D_1, 8.8% D_2, and 16.2% D_3). The niobium complex is inert to water but it was previously shown[1] to react with chlorine to give Me_3SiCH_2Cl and Me_3SiCl.

The carbyne compound could not be isolated from the interaction of WCl_6, WCl_5, or WCl_4 with $(Me_3SiCH_2)_2Mg$ in petroleum and only $(Me_3SiCH_2)_6W_2$ was obtained. By contrast, in tetrahydrofuran, WCl_6 and $(Me_3SiCH_2)_2Mg$ afford a red oil whose ^{1}H-NMR spectrum contains resonances attributable to both $(Me_3SiCH_2)_6W_2$ and the carbyne complex; however, chromatography in petroleum on neutral alumina yielded only the former.

It appears that ether solvents are of major importance in the deprotonation of the Me_3SiCH_2 group, possibly through increased basicity. Deprotonation of methylene groups has also been noted for tetrabenzyltitanium with tribenzylaluminum[5] and of a neopentyltantalum by neopentyllithium[6].

Experimental:

Bis(trimethylsilylmethyl)magnesium (10.3 ml of a 1.25 M diethyl ether solution, 13 mmol) was added to a suspension of WCl_4[7] (2.20 g, 0.0064 mol) in tetrahydrofuran (50 ml). After stirring 12 h all the WCl_4 appeared to dissolve. The volatile material was evaporated to dryness and heated (70—100 °C) in vacuum for 24 h. Extraction of the solid with petroleum (40—60 °C) yielded a brown-red solution which was filtered, concentrated to *ca.* 1 ml, and cooled (−70 °C). The brown-red polycrystalline, glass-like solid was collected and dried in vacuum: yield 0.5 g of $C_{24}H_{62}Si_6W_2$. The compound sublimes at 140—150 °C/10^{-3} torr.

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A CH-Carbene Complex of Iron by Metal-Induced Fragmentation of Two Bonds of a Bicyclopentane Unit[1]

By *Rudolf Aumann, Horst Wörmann,* and *Carl Krüger*[*]

The decomposition of intermediary metallacyclobutanes *(1)* to carbene complexes and olefins has been discussed as the decisive step of olefin metathesis[2].

A variant of this reaction sequence based on the model reaction *(4)* → *(5)* → *(7)* has been verified by isolation of organometallic intermediates. The carbon atoms corresponding to C_a, C_b, and C_c are indicated as dots in the formulas.

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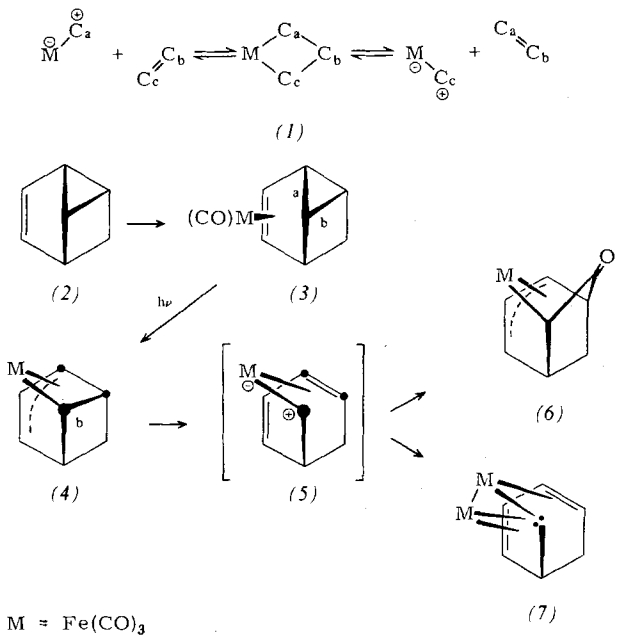
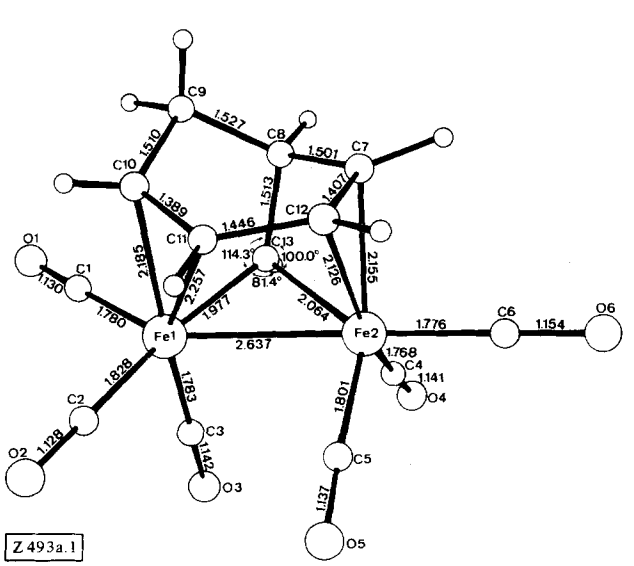


Low-temperature photolysis of $Fe(CO)_5$ in the presence of tricyclo[3.2.0.0^{2,7}]hept-3-ene *(2)*[3] affords the tetracarbonyl complex *(3)* as a yellow, thermolabile oil. On prolonged photolysis, *(3)* decomposes smoothly with loss of carbon monoxide and subsequent opening of bond a of the bicyclopentane unit to the π-allyl σ-complex *(4)*, whose acyl derivative can be isolated in crystalline form (21 %, m.p. 60 °C). (In the acyl derivative a carbonyl group is inserted in the Fe—C bond.) We have been able to show that the ketone complex *(6)* (*ca.* 95 %, m.p. 87.5 °C) is formed from *(4)* in the presence of free carbon monoxide at 20 °C. If, however, *(4)* or its acyl derivative is allowed to react with cyclohexene-$Fe(CO)_4$[4] at −20 °C, the dinuclear carbene complex *(7)* is obtained as main product (22 %, m.p. 98 °C) along with small amounts of *(6)*.

The ketone complex *(6)* is formed from a ketene precursor, which can be trapped as the methyl ester with methanol[5]. From the stereochemistry of the trapped product we believe that intermediary occurrence of the mononuclear carbene complex *(5)* can be concluded. *(5)* is a plausible precursor of the carbene complex *(7)* in which the carbene carbon is stabilized by two $Fe(CO)_3$ groups.

Stepwise transformation of the hydrocarbon *(2)* into the carbene complex *(7)* with cleavage of adjacent bonds[6] a and b of the bicyclopentane unit afforded evidence for the fragmentation of a metallacycle into a carbene and an olefin component, as has been postulated in the case of olefin metathesis. The structures of the complexes *(3)*, *(4)*, *(6)*, and *(7)* were determined on the basis of IR, ^{1}H-NMR, and ^{13}C-NMR measurements. In addition, a crystal structure analysis was carried out on the complex *(7)* (Fig. 1). The synthesis of *(7)* is the first example of the preparation of a hydrocarbon-carbene complex[6, 7] by metal-induced fragmentation of a strained hydrocarbon.

The bond length (2.63 Å) typical for carbene-bridged Fe—Fe bonds[9] is not further increased by the novel bridging of two iron atoms by a π-bonded, almost planar 1,3-diene unit (C10=C11—C12=C7) and also by the carbene carbon (C13). The Fe—$C_{carbene}$ distances are unequal [1.977(3), 2.064(3) Å] but both lie within the expected range[10]. $C_{carbene}$ occupies an apical position to the trigonal pyramidal Fe2 atom, and also a position in the trigonal plane of the similar type Fe1 atom. The same applies for the π-bonded part of the molecule. Hence different bonding (Fe—C10—C11 and Fe2—C7—C12) occurs in the π-bonded 1,3-diene system. The different Fe—$C_{carbene}$ distances are also understandable. Finally, they make a twisted arrangement of the two $Fe(CO)_3$ groups possible.



Z 493a.1

Fig. 1. Crystal structure of the dinuclear carbene complex *(7)*. $a = 19.273(3)$, $b = 13.858(1)$, $c = 10.2347(7)$ Å, space group Pbca, $Z = 8$, MoK_α radiation, 2940 reflections, of which 793 unobserved, $R = 0.0295$ ($R_w = 0.035$) [8].

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German version: Angew. Chem. *88*, 640 (1976)

CAS Registry numbers:
$Fe(CO)_5$, 13463-40-6; *(2)*, 6006-21-9; *(3)*, 60064-64-4; *(4)*, 60064-65-5; *(6)*, 60064-66-6; *(7)*, 60064-67-7

[1] Reactions of Strained C—C Single Bonds with Transition Metals, Part 14. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 13: *R. Aumann*, Chem. Ber. *109*, 168 (1976).
[2] *C. P. Casey* and *T. J. Burkhardt*, J. Am. Chem. Soc. *96*, 7809 (1974); *R. H. Grubbs*, *P. L. Burk*, and *D. D. Carr*, *ibid.* *97*, 3265 (1975); *T. J. Katz* and *J. McGinnis*, *ibid.* *97*, 1593 (1975); *M. T. Mocella*, *M. A. Busch*, and *E. L. Muetterties*, *ibid.* *98*, 1284 (1976); cf. *N. Calderon*, *E. A. Ofstead*, and *W. A. Judy*, Angew. Chem. *88*, 433 (1976); Angew. Chem. Int. Ed. Engl. *15*, 401 (1976).
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Oxidative Addition of the Central Bond of a Bicyclopentane System to Iron[1]

By *Rudolf Aumann* and *Heinz Averbeck*[*]

An *exo* attack of the metal on the bridge of the bicyclic system[4] is postulated as the primary step in transition-metal catalyzed isomerizations[2] or cycloadditions of bicyclo[2.1.0]-pentanes to olefins[3]. We have now succeeded in isolating stable iron complexes arising from such an attack.

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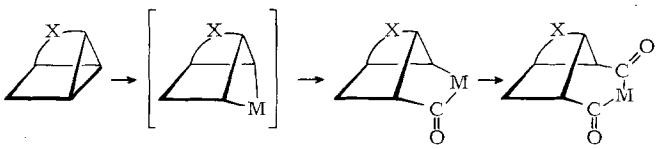
The light-induced reaction of hydrocarbons *(1a)* and *(1b)* with pentacarbonyliron (20°C, ether, Hg high-pressure lamp, 20 and 3h, respectively) yields the colorless tetracarbonylferrapolycyclics *(3a)* (37%, m.p. 115°C, IR ν(M)—C≡O: 2099, 2040, 2026, 2016 cm^{-1}, νC=O 1673 cm^{-1}) and *(3b)* (85% m.p. 96°C, IR ν(M)—C≡O: 2097, 2037, 2020, 2012 cm^{-1}, νC=O 1673 cm^{-1}), which further react with carbon monoxide smoothly to the bis(acyl) compounds *(4a)* (*ca.* 95%, slow decomposition above 100°C, IR ν(M)—C≡O: 2108, 2052, 2050, 2016 cm^{-1}, νC=O 1634 cm^{-1}) and *(4b)* (*ca.* 95%, slow decomposition above 85°C, IR ν(M)—C≡O: 2106, 2050, 2047, 2013 cm^{-1}, νC=O 1633 cm^{-1}).



(1) *(2)* *(3)* *(4)*

M = $Fe(CO)_4$; *a* X = ; *b* X =

The methanotetrahydronaphthalene moiety of *(3a)* could be identified on the basis of experimentally determined proton coupling constants refined by computer simulation (Fig. 1). In accord with the proposed structure, on addition of $Eu(fod)_3$ to a C_6H_6 solution of the compound the resonance signals at $\delta_{TMS}=2.35$, 1.90, 3.23 ppm are the most strongly shifted to low field.

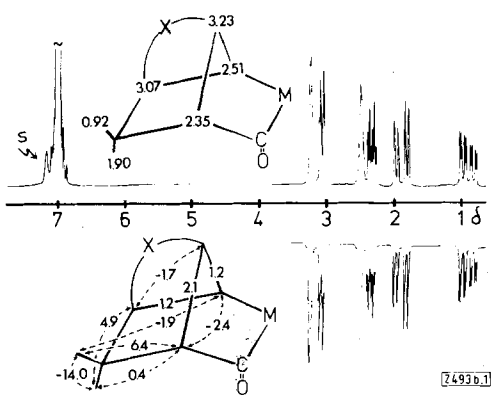


Fig. 1. ^{1}H-NMR spectrum of *(3a)* (C_6D_6, 90 MHz). Above: experimental, below: computer-simulated spectrum using the quoted parameters (δ values, coupling constants in Hz). S = solvent.

According to ^{1}H-NMR measurements compounds *(3b)*, *(4a)*, and *(4b)* contain the same structural elements as *(3a)*.

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CAS Registry numbers:
(1a), 7213-64-1; *(1b)*, 279-18-5; *(3a)*, 60064-56-4; *(3b)*, 60064-57-5; *(4a)*, 60064-58-6; *(4b)*, 60064-59-7; $Fe(CO)_5$, 13463-40-6

[1] Reactions of Strained C—C Single Bonds with Transition Metals, Part 15. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 14: *R. Aumann, H. Wörmann*, and *C. Krüger*, Angew. Chem. *88*, 640 (1976); Angew. Chem. Int. Ed. Engl. *15*, 609 (1976).

[2] a) *K. B. Wiberg* and *K. C. Bishop, III*, Tetrahedron Lett. *1973*, 2727; b) *M. A. McKinney* and *S. K. Chou, ibid. 1974*, 1145; c) *P. G. Gassman, T. J. Atkins*, and *J. T. Lumb*, J. Am. Chem. Soc. *94*, 7757 (1972).

[3] *R. Noyori, Y. Kumagai*, and *H. Takaya*, J. Am. Chem. Soc. *96*, 634 (1974).

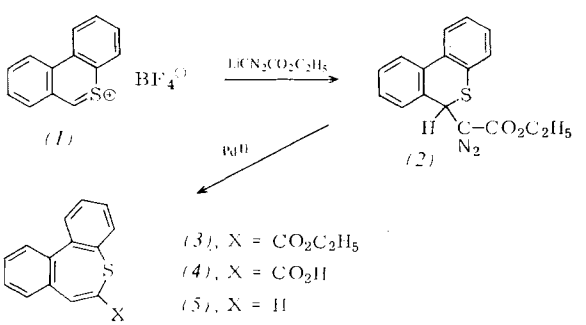
[4] A strain energy of *ca.* 47 kcal/mol should be released on cleavage of this bond; cf. *R. B. Turner, P. Goebel, B. J. Mallon, W. v. E. Doering, J. F. Coburn, Jr.*, and *M. Pomerantz*, J. Am. Chem. Soc. *90*, 4315 (1968); *S. Chang, D. McNally, S. Shary-Tehrany, M. J. Hickey*, and *R. H. Boyd, ibid. 92*, 3109 (1970).

New Synthetic Entry to the Thiepin System.—Benzo[*d*]thiepin and Dibenzo[*bd*]thiepin

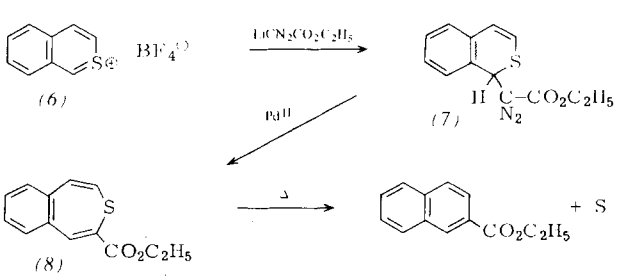
By *Kazuhiro Nakasuji, Koichi Kawamura, Toshio Ishihara*, and *Ichiro Murata*[*]

Because of the ease of sulfur extrusion, extremely mild conditions have to be employed for synthesis of the thiepin system. We have previously found it possible to prepare benzo[*b*]thiepin[1] by Rh^I-catalyzed isomerization of 6-thiatetracyclo[5.4.0.$0^{2,4}$.$0^{3,5}$]undeca-1(7),8,10-triene[2], a valence isomer of benzo[*b*]thiepin, under mild condition. We now describe the synthesis of benzo[*d*]- and dibenzo[*bd*]thiepin systems.

The readily accessible dibenzothiopyrylium tetrafluoroborate *(1)*[3] reacts with ethyl lithiodiazoacetate[4] in a 1:1 mixture of diethyl ether and tetrahydrofuran at −120°C to form diazo compound *(2)* [yellow oil, 32% yield]. Treatment of *(2)* with π-allylpalladium chloride dimer (5 mole %) in a 1:2 mixture of chloroform and carbon tetrachloride at 0°C and allowing to warm to room temperature for 2h affords the desired 6-ethoxycarbonyldibenzo[*bd*]thiepin *(3)*[5] quantitatively as a pale yellow oil. The spectra of *(3)* was fully consistent with the thiepin structure. Despite the presence of the thiepin skeleton, *(3)* is a stable compound and fails to transform into 9-ethoxycarbonylphenanthrene even at elevated temperature in the presence of triphenylphosphane. Alkaline hydrolysis of *(3)* gives the free acid *(4)* [pale yellow plates, m.p. 220°C (dec.), 93% yield]. Decarboxylation of *(4)* with copper in quinoline at 150°C for 30 min leads to the parent dibenzo[*bd*]thiepin *(5)* (colorless plates, m.p. 82 to 83°C) which on thermolysis in refluxing xylene in the presence of triphenylphosphane for 1 day furnishes phenanthrene.



The synthetic utility of the ring enlargement reaction was illustrated by its application to the diazo compound *(7)* [yellow oil, 53% yield] which was prepared from benzothiopyrylium tetrafluoroborate *(6)*[6]. When *(7)* was subjected to reaction with π-allylpalladium chloride dimer under the same condition as in the case of *(2)*, the product isolated was



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ethyl β-naphthoate. However, treatment of *(7)* with the Pd-catalyst at −10 °C for 2 h followed by low temperature column chromatography on silica gel (deactivated with 6% water) at −40 °C with a 1:10 mixture of diethyl ether and light petroleum provides pure *(8)*. The structure assignment for *(8)* was based on its ^{1}H-NMR data. Thermal transformation of *(8)* into naphthalene and sulfur was monitored by ^{1}H-NMR and the half-life of *(8)* was found to be 54 min at 24 °C.

Table 1. Spectral data of compounds *(2)*, *(3)*, *(5)*, *(7)* and *(8)*.

(2): IR (CCl_4): $\nu_{C=O}$ = 1690 cm^{-1}, ν_{N_2} = 2080; ^{1}H-NMR (CCl_4): δ = 1.23 (t, J = 7.0 Hz, 3H), 4.18 (q, J = 7.0 Hz, 2H), 4.97 (s, 1H), 7.1—7.5 (m, 6H), 7.6—7.8 (m, 2H).

(3): IR (neat): $\nu_{C=O}$ = 1710 cm^{-1}; UV (cyclohexane): λ_{max} = 213 nm (log ε = 4.33), 245 (4.41), 260 (s, 4.29), 346 (3.41); ^{1}H-NMR (CCl_4): δ = 1.35 (t, J = 8.0 Hz, 3H), 4.33 (q, J = 8.0 Hz, 2H), 8.07 (s, 1H), 7.2—7.7 (m, 8H).

(5): UV (cyclohexane): λ_{max} = 213 nm (s, log ε = 4.39), 229 (4.48), 260 (s, 4.15), 300 (s, 3.06); ^{1}H-NMR ($CDCl_3$): δ = AB-q 6.57 and 7.00 (J_{AB} = 9.0 Hz), 7.2—7.6 (m, 8H).

(7): IR (CCl_4): $\nu_{C=O}$ = 1690 cm^{-1}, ν_{N_2} = 2080; ^{1}H-NMR (CCl_4): δ = 1.27 (t, J = 7.0 Hz, 3H), 4.21 (q, J = 7.0 Hz, 2H), 5.00 (d, J = 1.8 Hz, 1H), 6.39 (dd, J = 9.5, 1.8 Hz, 1H), 6.61 (d, J = 9.5 Hz, 1H), 7.2 (m, 4H).

(8): ^{1}H-NMR (−60 °C, $CDCl_3$ + CCl_4): δ = 1.30 (t, J = 7.0 Hz, 3H), 4.31 (q, J = 7.0 Hz, 2H), AB-q 6.07 and 6.93 (J_{AB} = 9.0 Hz), 8.00 (s, 1H), 7.3 (m, 4H).

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CAS Registry numbers:
(1), 59991-94-5; *(2)*, 59991-95-6; *(3)*, 59991-96-7; *(4)* 59991-97-8; *(5)*, 220-07-5; *(6)*, 3481-78-5; *(7)*, 59991-98-9; *(8)*, 59991-99-0

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[5] Satisfactory elemental analyses were obtained for *(3)*, *(4)*, and *(5)*. Compound *(8)* could not be analyzed due to its thermal instability.
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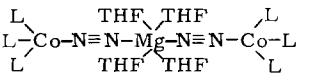
A Novel Hetero-Bimetallic Dinitrogen Complex[**]

By *Reinhard Hammer, Hans-Friedrich Klein, Ulrich Schubert, Albin Frank*, and *Gottfried Huttner*[*]

Phosphane complexes of cobalt in low oxidation states show a tendency to take up molecular nitrogen[1]. It therefore appeared somewhat surprising that the compounds L_4CoH[2] and L_4Co[3,4] [L = $(CH_3)_3P$] failed to show such a tendency.

We have now found that the generally smooth reduction of $CoCl_2/(CH_3)_3P$ in tetrahydrofuran by magnesium turnings[4] under N_2 as protective gas, which yields L_4Co, can be induced to undergo an unusual further step under modified conditions: with a fivefold excess of magnesium and longer reaction times (3 d, 20 °C) the dark brown solution reproducibly lightens to orange yellow. Extraction of the residue with pentane/THF (50:1) furnishes good yields (70%) of an orange diamagnetic compound *(1)* [dec. > 82 °C, ν(N≡N): 2068 cm^{-1} in hexane, 2058 cm^{-1} in THF] whose crystals effloresce in a vacuum and in a current of N_2.



(1), L = $(CH_3)_3P$

In the absence of a clean magnesium surface L_4Co fails to take up molecular nitrogen; tetrahydrofuran cannot be replaced by other O donors (ether, dioxane, glycol dimethyl ether). Moreover, solutions of $NaCoL_4$ or $KCoL_4$ in these ethers do not take up any nitrogen, while lithium metal, which like magnesium reacts with N_2 at room temperature, does permit incorporation of N_2 on reduction of L_4Co. The activation of the molecular nitrogen by reactive metal surfaces must therefore be of crucial importance.

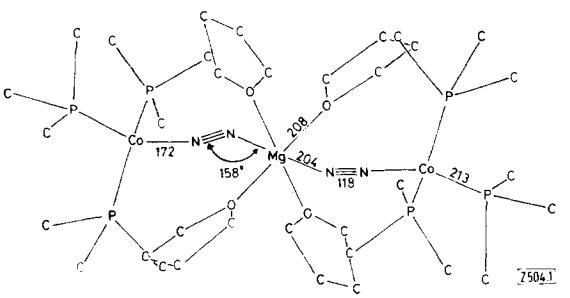


Fig. 1. Crystal structure of *(1)*[5]. Bond lengths in pm.

The structure of compound *(1)* was determined by X-ray methods (Fig. 1). *(1)* contains a center of symmetry. An octahedrally coordinated magnesium atom in the center of the complex bears four equatorial tetrahydrofuran ligands. The axial positions of the coordination octahedron are occupied by N_2 groups which are each simultaneously bound as bridging ligands to a $(Me_3P)_3Co$ unit. The Mg—N—N—Co grouping is bent at the nitrogen bonded to the magnesium (158°). Like the relatively long N—N distance (118 pm), this indicates a significant change in the bonding on going from free to complexed N_2. The other bond lengths and angles correspond to the usual values[6].

The composition of *(1)* shows some resemblance to a class of new alkali metal dinitrogen complexes discovered by *K. Jonas*[7]; however, *(1)* contains end-on N_2 bridges between a transition metal and an electropositive main group element.

In solvents of low polarity (pentane, benzene, toluene) *(1)* decomposes with deposition of metal and evolution of nitrogen to form L_4Co. A freshly prepared solution (0.1% in toluene, frozen to a glass at 77 K) already displays the EPR spectrum of L_4Co[3]. However, dilute THF solutions are also paramagnetic: their EPR signal (77 K) consists of a broad Lorentzian line (g = 2.059, half-width 160 G) with four of eight hyperfine lines (^{57}Co, I = 7/2, A^{Co} = 90 G) being recognizable on the high field side. We assign this signal to dinitrogentris(trimethylphosphane)cobalt(0) *(2)*, whose presence in solution is also indicated by the smooth substitution reactions occurring with π-acceptor ligands according to eq. (a).

$$[L_3CoN_2] + 2\,L' \longrightarrow L_2CoL'_2 + N_2 + L \qquad (a)$$

(2)

L = $(CH_3)_3P$

2 L' = $C_6H_5N{=}NC_6H_5$, $C_6H_5CH{=}CHC_6H_5$, 2,2'-bipyridyl, 2 CO

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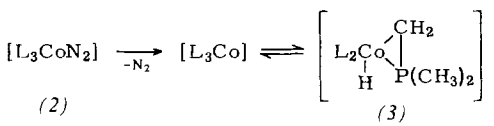
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

The IR spectrum of a Nujol mull of *(1)* suggests that N_2 elimination is followed initially by stabilization of the L_3Co fragment such as in *(3)*, because the ν(CoH) band grows at the expense of the ν(NN) band, and then by formation of L_4Co.



(2) *(3)*

ν(NN) = 2064 cm^{-1} ν(CoH) = 1830 cm^{-1} (br)

Reversible filling of a coordination vacancy on the metal by C—H cleavage of a trimethylphosphane ligand is not without precedent[8]; nor is a CoCP three-membered ring[9].

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German version: Angew. Chem. *88*, 648 (1976)

CAS Registry numbers:
(1), 60184-44-3; *(2)*, 60184-46-5; *(3)*, 60184-43-2; $[P(CH_3)_3]_2Co(C_6H_5N{=}NC_6H_5)$, 33152-39-5; $[P(CH_3)_3]_2Co(C_6H_5CH{=}CHC_6H_5)$, 60195-78-0; $[P(CH_3)_3]_2Co$(2,2'-bipyridyl), 60184-47-6; $CoCl_2$, 7646-79-9; $P(CH_3)_3$, 594-09-2; Mg, 7439-95-4; N_2, 7727-37-9; $[P(CH_3)_3]_2Co(CO)_2$, 60184-45-4

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[2] *H.-F. Klein*, Angew. Chem. *82*, 885 (1970); Angew. Chem. Int. Ed. Engl. *9*, 903 (1970).
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[4] *H.-F. Klein* and *H. H. Karsch*, Chem. Ber. *108*, 944 (1975).
[5] Data collected at −70°C on a SYNTEX P2$_1$ diffractometer; Solution (R_1 = 0.076) on a SYNTEX-XTL structure solving system.
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[7] *K. Jonas*, Angew. Chem. *88*, 51 (1976); Angew. Chem. Int. Ed. Engl. *15*, 47 (1976), and references cited therein.
[8] *H. H. Karsch, H.-F. Klein*, and *H. Schmidbaur*, Angew. Chem. *87*, 630 (1975); Angew. Chem. Int. Ed. Engl. *14*, 637 (1975).
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1*H*-Cyclopropa[*a*]naphthalene from 2,3-Benzo-1,6-methano[10]annulene

By *Shigeo Tanimoto, Rainer Schäfer, Joachim Ippen*, and *Emanuel Vogel*[*]

Dedicated to Professor Leonhard Birkofer on the occasion of his 65th birthday

1*H*-Cyclopropa[*a*]naphthalene *(1)* and 1*H*-cyclopropa[*b*]naphthalene *(2)* warrant interest with regard to the possibility of localizing the bonds of aromatic nuclei by annelation of three-membered rings. While *(2)* has recently been prepared by dehydrohalogenation of 7,7-dichloro-3,4-benzonorcarene[1], *(1)* has hitherto remained unknown.

The synthesis of *(1)* has now been accomplished starting from 2,3-benzo-1,6-methano[10]annulene *(4)*, which is also described in this communication for the first time, by Diels-Alder reaction and Alder-Rickert cleavage[2].

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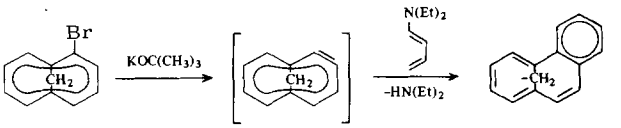
(1) *(2)*

2,3-Benzo-1,6-methano[10]annulene *(4)* is obtained on heating a mixture of 2-bromo-1,6-methano[10]annulene *(3)* and *N*,*N*-diethyl-1,3-butadienylamine (8-fold excess) with potassium *tert*-butoxide (6-fold excess) in toluene with stirring (105°C; 15 h), chromatographing with pentane over silica gel, and recrystallizing from pentane (cooling to −35°C). The yield of *(4)* (pale yellow needles, m.p. 47–48°C) is 20%.



(3) *(4)*

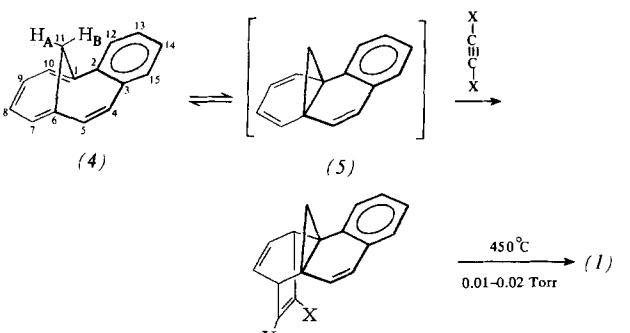
Although the ^{1}H-NMR spectrum (100 MHz; [D_6]acetone) of *(4)* is relatively complex, the observed coupling and a comparison with the spectra of the 5,7,10-trideuterio compound[3] and of phenanthrene permit the following assignment of the resonance signals: τ = 2.96 (H_4), 2.67 (H_5), 3.01 (H_7), 2.74 (H_8, H_9), 2.66 (H_{10}), 1.66 (H_{12}), 2.50 (H_{13}), 2.45 (H_{14}), 2.15 (H_{15}), 8.62 (H_{11B}), and 10.06 (H_{11A}); $J_{4,5}$ = 11.05 Hz, $J_{11A,11B}$ = 9.0 Hz[4].

The ^{1}H-NMR data and the ^{13}C-NMR spectrum provide no indication of an equilibrium between *(4)* and its norcaradiene valence tautomer *(5)*.

The weakening of the diamagnetic ring current in the [10]annulene ring of *(4)* expected as a result of benzo-annelation is most clearly manifested in the resonance signals of the bridge protons for they are shifted 1.9 and 0.5 ppm, respectively, downfield relative to those in 1,6-methano[10]annulene[5]. More subtle NMR findings such as the relatively large vicinal coupling constant $J_{4,5}$, the relation $\tau(H_7) > \tau(H_8)$[5], and the chemical shift difference of the bridge protons [$\tau(H_{11A}) \gg \tau(H_{11B})$] even suggest that the π bonds in the [10]annulene ring are largely localized according to the cycloheptatriene canonical structure *(4)*.

In accord with the π-electron structure deduced from the NMR spectrum, *(4)* reacts in boiling benzene (3 h) with dicyanoacetylene, giving an almost quantitative yield of the adduct *(6a)* [colorless crystals, m.p. 183—184°C (from ethanol)]. Reaction with dimethyl acetylenedicarboxylate in benzene at 120°C (10 h) affords *(6b)*, m.p. 147—148°C (from *n*-hexane).

The adducts *(6a)* and *(6b)* decompose uniformly and completely to give 1*H*-cyclopropa[*a*]naphthalene *(1)* and phthalodinitrile and dimethyl phthalate, respectively, on pyrolysis at 450°C and 0.01 to 0.02 torr in a quartz tube (length 40 cm,



(4) *(5)*

(6a), X = CN
(6b), X = CO_2CH_3

i. d. 5 mm). After chromatography over alumina (Brockmann) with pentane (argon atmosphere; −20 °C) and crystallization from pentane at −78 °C, *(1)* is obtained as nacreous colorless platelets of m. p. 19—20 °C (partial polymerization or decomposition); yields: 68 % from *(6a)*, 83 % from *(6b)*[6].

The ^{1}H-NMR spectrum (60 MHz; CCl_4; −20 °C) of *(1)* shows a complex multiplet at $\tau = 2.00$ to 2.76 (6 aromatic protons), in which an AB system can be made out at $\tau = 2.32$ (H_3) and 2.57 (H_2), $J_{2,3} = 6.9$ Hz, and a singlet at $\tau = 6.58$ (CH_2 protons). The spectrum corresponds to that of the isomer *(2)*, especially in the finding that the protons of the benzene ring adjacent to the three-membered ring absorb in the range for aromatic protons. Since $J_{2,3}$ also agrees in magnitude with the vicinal coupling constant $J_{1,2}$ (8.28 Hz) of naphthalene[7], a significant degree of bond fixation appears just as improbable in *(1)* as in *(2)*.

Apart from the above reasoning, the UV spectrum of *(1)* justifies our regarding the hydrocarbon as a derivative of naphthalene. Furthermore, the other spectra all document the close resemblance between *(1)* and *(2)* rather than revealing any bonding anomalies due to ring strain.

As in *(2)* and cyclopropabenzene, the three-membered ring of *(1)* undergoes solvolytic cleavage at one of the CH_2—C bonds when the molecule is exposed to the catalytic action of H^+ and Ag^+ ions.

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CAS Registry numbers:
(1), 277-43-0; *(3)*, 15825-92-0; *(4)*, 13352-41-5; *(6a)*, 60084-53-9; *(6b)*, 60084-54-0; *N,N*-diethyl-1,3-butadienylamine, 14958-13-5; dicyanoacetylene, 1071-98-3; dimethyl acetylenedicarboxylate, 762-42-5

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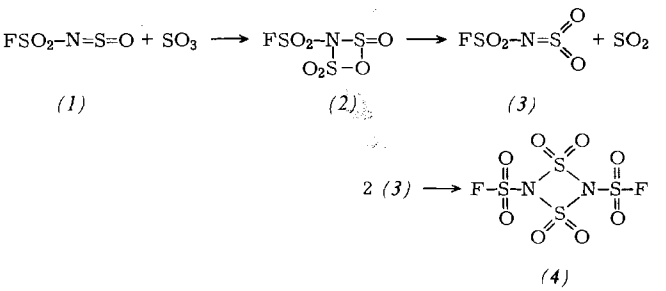
[3] 5,7,10-Trideuterio-2,3-benzo-1,6-methano[10]annulene was prepared from 2,5,7,10-tetradeuterio-1,6-methano[10]annulene (*E. Vogel*, Special Publication *21*, 113, The Chemical Society, London 1967) in the same way as *(4)*.
[4] A detailed account of the NMR spectra of 2,3-benzo-1,6-methano[10]annulene *(4)* and 3,4-benzo-1,6-methano[10]annulene (*R. Schäfer*, Dissertation, Universität Köln 1974) will be published jointly with *H. Günther* and *H. Schmickler*.
[5] *H. Günther*, Z. Naturforsch. *20b*, 948 (1965).
[6] An alternative synthesis of *(1)* was accomplished simultaneously by *K. Grohmann*, Department of Chemistry, Hunter College, New York (personal communication).
[7] *J. B. Pawliczek* and *H. Günther*, Tetrahedron *26*, 1755 (1970).

A New Cyclic SN Compound: 1,1,3,3-Tetraoxo-2,4-difluorosulfonylcyclodiaza-λ^6-thiane[**]

By *Klaus-Dieter Schmidt, Rüdiger Mews*, and *Oskar Glemser*[*]

N-(Fluorosulfonyl)sulfur oxide imide *(1)*[1] reacts with sulfur trioxide to give the cyclic end product *(4)*. On the basis of the results obtained in other studies[2] we assume that the reaction proceeds in analogy with the formation of sultones. In contrast to the reaction of $FCONSF_2$ with SO_3[2b], in which the β-sultone could be isolated, sultone *(2)* immediately decomposes with elimination of sulfur dioxide, which was detected by IR spectroscopy. The primary product *(3)*, formally a derivative of sulfimide, appears to be unstable as the monomer; it immediately dimerizes to *(4)*.



The composition and structure of the compound are confirmed by elemental analysis, characteristic fragments in the mass spectrum, and by its IR and Raman spectra. Compound *(4)* is a water-clear liquid (m.p. +16.5 °C) which fumes profusely on exposure to air and reacts vigorously with organic compounds. Decomposition sets in on warming to above 30 °C.

$(FSO_2NSO_2)_2$ represents a new type of the extremely rare four-membered SN ring system. Among the other members, the planar[3] S_2N_2[4] and its addition compounds $S_2N_2 \cdot A$ ($A = SbCl_5$, BCl_3)[5] have been known for some time. Less certainty surrounds the existence of $S_2N_2 \cdot R_2$ (R = *tert*-butyl)[6], while $(F_3C—S{=}N)_2$ can be prepared only with difficulty and in very small amounts[7]. Apart from the present four-membered ring with $n = 2$, other known representatives of the $(RNSO_2)_n$ type include higher-membered rings with $n = 3$ or 4 ($R = CH_3$ *etc.*)[8] and $n = 6$ in $(HNSO_2)_6$[9].

1,1,3,3-Tetraoxo-2,4-difluorosulfonylcyclodiaza-λ^6-thiane (4)

All operations were performed in carefully dried glass apparatus with exclusion of atmospheric moisture.

Stabilized SO_3 (66.7 g, 0.833 mol) is added dropwise to ice-cooled FSO_2NSO (120.8 g, 0.833 mol) and the reaction mixture slowly allowed to warm up to room temperature. In the course of several days SO_2 (49.8 g) condenses in the protective trap. The reaction mixture is subjected to N_2 pressure filtration, and on subsequent low-temperature vacuum condensation of the liquid phase product *(4)* collects in a trap cooled to −20 °C. Repeated distillation affords the pure compound (107.9 g, 0.34 mol; 80 %).

IR spectrum (CaF_2 plates were used because the substance reacts with KBr and NaCl; capillary film) [cm^{-1}]: 1490 vs, 1450 vs, 1330 w, 1230 vs, 1205 vs.—Raman spectrum [cm^{-1}]: 1494 w (br), 1445 w (br), 1372 vw, 1263 vs, 1247 w, 1218 w, 915 vw, 847 w (br), 832 w, 803 w (br), 659 vs, 576 w, 541 w, 517 vw, 472 w, 454 w, 432 w, 383 w, 338 vs, 324 w, 278 s, 261 m, 216 s, 179 w, 135 w.—Mass spectrum (*m/e*): 322 M^+ (16 %), 161 FSO_2NSO_2 (100 %), 142 SO_2NSO_2 (20 %), 83 FSO_2 (58 %), 67 SOF (10 %), 64 SO_2 (49 %), 48 SO (20 %), 46 NS (5 %).—^{19}F-NMR spectrum: $\delta_{SF} = -58.7$ ppm (relative to $CFCl_3$ as external standard).

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CAS Registry numbers:
(1), 16829-30-4; *(4)*, 60153-70-0; SO_3, 7446-11-9

[1] *H. W. Roesky*, Angew. Chem. *79*, 724 (1967); Angew. Chem. Int. Ed. Engl. *6*, 711 (1967).
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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

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Molecular Structure of $C_5H_5Mn(CO)_2[(C_6H_5)_2C{=}C{=}O]$. — Out-of-Plane Deformation of the Diphenylketene Ligand[1]

By *A. D. Redhouse* and *W. A. Herrmann*[*]

Structural data for metal complexes containing heterocumulenes as ligands are known in only a few cases. In the diphenylketene complexes $(\eta\text{-}C_5H_4R)Mn(CO)_2[(C_6H_5)_2C{=}C{=}O]$ (R = H: *(1)*; R = CH_3: *(2)*) spectroscopic as well as chemical evidence indicates that the "heterocumulene" is bound to the metal *via* a π-olefin system without the participation of the carbonyl oxygen[2]. X-Ray structure determination of *(1)* revealed for the first time the structural parameters of a coordinated ketene. We solved the structure using heavy atom procedures based on 686 independent non-zero reflections (Mo-K_γ radiation, microdensitometer techniques[3]) and refined it by least-squares methods to a conventional *R* value of 0.083.

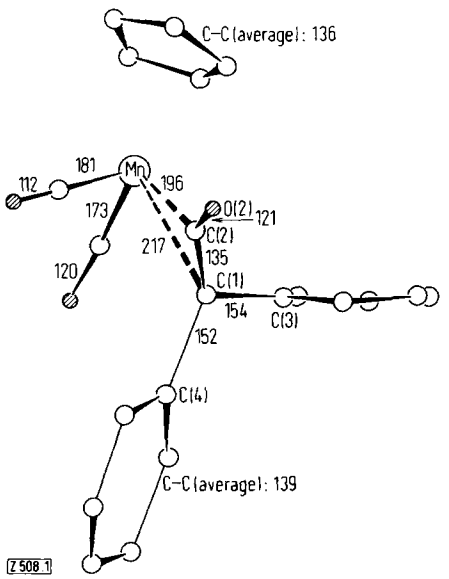


Fig. 1. Molecular structure of dicarbonyl(η-cyclopentadienyl)(diphenylketene)manganese *(1)*; bond lengths in pm. —Crystal data: $C_{21}H_{15}MnO_3$, rel. molecular weight 370.3, dark yellow monoclinic crystals from *n*-hexane/diethylether (5:2, −35 °C), $a = 678(2)$ pm, $b = 1397(2)$ pm, $c = 1863(2)$ pm, $\beta = 99.55°$, $d_m = 1.40$ g cm^{-3}, $d_{calc} = 1.41$ g cm^{-3} for $Z = 4$, space group $P2_1/c$.

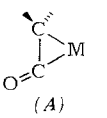
The following structural data are characteristic for the diphenylketene ligand in *(1)* (cf. Fig. 1):

1) The heterocumulene framework is no longer linear in the complex molecule (∢C(1)C(2)O(2) = 145°). It should be noted that this is an out-of-plane deformation, the dihedral angle between the plane defined by C(1), C(2), C(3), and C(4) and the plane defined by C(1), C(2), and O(2) being 89°.

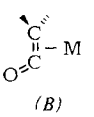
2) The C(1)—C(2) distance of 135(2) pm is not only typical of a C=C double bond but also greater than that found in free ketenes (*e.g.* dimethylketene[4]: 127.1 pm). In contrast, the C=O bond length of the ketene carbonyl group is not affected significantly on coordination of the ligand (dimethylketene[4]: 117.9 pm; complex *(1)*: 121(2) pm).

3) The distances of the carbon atoms C(1) and C(2) from the metal atom are clearly different from each other (217(2) and 196(2) pm, respectively). This could be the result of steric interactions between one of the two phenyl rings and the metal carbonyl groups. On the other hand, the Mn—C(1) distance compares favorably with values found for typical Mn—C(π-olefin) systems such as $C_5H_5Mn(CO)_2$(norbornadiene) (217 pm)[5a] or $C_5H_5Mn(CO)_2$(methylvinylketone) (214.9—217.5 pm)[5b], whereas Mn—C(2) is by comparison very short.

The considerable deviation of the ligand from linearity suggests an alternative formulation of *(1)* and *(2)* as "metallacyclopropanone" systems *(A)* as proposed by *Beck et al.* for the platinum complex $[P(C_6H_5)_3]_2Pt[(C_6H_5)_2C{=}C{=}O]$[6]. Both models *(A)* and *(B)* represent extreme descriptions of the bonding of unsaturated systems in metal complexes.



(A)



(B)

The overall geometry of the coordinated ketene is very similar to that of coordinated carbon dioxide and carbon disulfide ligands[7], which are also nonlinear. The bonding in these complexes has been interpreted in terms of the geometry of an excited state of the ligand. However, there is no excited state in which ketene has an out-of-plane deformation and at the same time a short C=C distance. The first excited state $^3A'$ ($^3A_1$) for ketene with an out-of-plane deformation possesses an extremely long C—C distance (154 pm) as well as a small CCO angle (123°)[8a]. Interpretation of the transition metal—ketene bond in terms of the excited state of the ketene does not therefore seem possible.

Coordination of the heterocumulene gives rise to characteristic changes in the ^{13}C-NMR parameters too (Table 1): The

Table 1. ^{13}C-NMR parameters of free and complexed diphenylketene [a].

	δ(C1)	δ(C2)	δ(M—CO)	δ(C_5H_4R)	δ(CH_3)	δ(C_6H_5)			
						C_1	C_o	C_m	C_p
$(C_6H_5)_2C{=}C{=}O$ (= L)	47.0 [8b]	201.3 [8b]	—	—	—	131.4	129.9	128.3	126.9
$C_5H_5Mn(CO)_2L$ *(1)*	− 4.1	237.5	238.0	89.0	—	141.8	129.4	128.8	126.3
$C_5H_4CH_3Mn(CO)_2L$ *(2)* [b]	− 5.1	236.4	238.5	89.6 (CH) [c] 105.6 (CCH_3)	12.7	142.8	129.6	129.1	126.3

[a] Spectrometer JOEL JNM-PS-100; recording temperature 27 °C; ^1H broad-band decoupled PFT spectra; *ca.* 1 M solutions in $CDCl_3$; δ-values (ppm) relative to internal TMS.
[b] In [D_6]acetone.
[c] In CD_2Cl_2: 89.4 and 89.3 (CH); 105.4 (CCH_3).

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resonance of the terminal carbon atom C(1) is shifted to higher field by *ca.* 50 ppm, whereas the carbonyl carbon atom becomes deshielded, and very much resembles, in terms of chemical shifts, metal carbonyl groups.

If the coordinated diphenylketene is formally considered as a bidentate ligand, the structural analogy of *(1)* and *(2)* with the square-pyramidal asymmetric compounds of the type $C_5H_5M(CO)_2(L—L')$ (M = Mo, W; L—L' = N—N'- and N—C-chelate ligands) first described by *Brunner*[9] becomes apparent. The chiral environment of the central metal in *(1)* and *(2)* should be detectable, for instance, by NMR spectroscopy. The ^{13}C-NMR spectra (Table 1) exhibit between −55 °C and room temperature only *one* signal for the terminal M—CO groups. Both the phenyl groups are seen to possess identical signals for corresponding ring positions. The diastereotopic effect upon the α- and β-C-positions in the cyclopentadienyl ring of *(2)*, expected on the basis of molecular asymmetry, is not observed. This indicates that the enantiomeric forms of the diphenylketene complexes undergo fast [NMR time scale] equilibration *via* symmetrical transition states[10].

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CAS Registry numbers:
(1), 53265-44-4; *(2)*, 53265-43-3; ^{13}C, 14762-74-4

[1] Communication 15 on Complex Chemistry of Reactive Organic Compounds.—Communication 14: *W. A. Herrmann* and *H. Biersack*, Chem. Ber., in press.
[2] *W. A. Herrmann*, Angew. Chem. *86*, 345 (1974); Angew. Chem. Int. Ed. Engl. *13*, 335 (1974).
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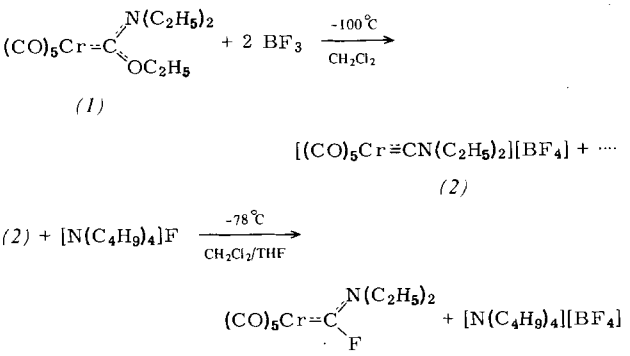
Pentacarbonyl(diethylaminofluorocarbene)chromium[1]

By *Ernst Otto Fischer, Willi Kleine*, and *Fritz Roland Kreissl*[*]

In analogy with the preparation of pentacarbonyl(diethylaminochlorocarbene)chromium[2], we attempted to prepare the first fluorocarbene complex by passing boron trifluoride into a solution of pentacarbonyl(diethylaminoethoxycarbene)chromium *(1)*[3], but only succeeded in initially isolating pentacarbonyl(diethylaminocarbyne)chromium tetrafluoroborate *(2)* as dark red crystals sensitive to air and heat. However, on reaction of this compound with tetrabutylammonium fluoride we obtained yellow crystalline pentacarbonyl(diethylaminofluorocarbene)chromium *(3)*, m.p. 40 °C.



Compositions and structures of the new complexes *(2)* and *(3)* are confirmed by elemental analysis and spectroscopic studies.

In the ν_{CO} range the IR spectra of *(1)*, *(2)*, and *(3)* (solution in CH_2Cl_2) show two absorptions corresponding to a $Cr(CO)_5$ group having pseudo-C_{4v} symmetry; relative to the carbene complexes *(1)* and *(3)* (2053 w, 1920 vs and 2064 w, 1930 vs cm^{-1}, respectively) the two bands of the carbyne complex *(2)* (2132 w, 2024 vs cm^{-1}) are shifted considerably to shorter wavelengths as a result of the positive charge.

In the ^1H-NMR spectrum the diethylamino group of *(2)* gives rise to a quartet and a triplet in the intensity ratio 4:6 (Table 1). On conversion of *(2)* into the fluorocarbene complex *(3)* the two *N*-ethyl groups are fixed in different environments owing to a p_π-p_π double bond component between the carbene carbon and the nitrogen atom[4], thus leading to signal splitting; a further splitting of the *N*-methylene protons in the *Z* position is due to interaction with the fluorine atom.

Table 1. ^1H-NMR spectra of complexes *(2)* and *(3)* in [D$_6$]acetone at −20 °C; δ values in ppm relative to CHD_2COCD_3 = 2.03 ppm.

	NCH_2 (*E*)	NCH_2 (*Z*)	NCH_2CH_3 (*E*,*Z*)
(2)	*3.98 (q)*		*1.53 (t)*
(3)	4.36 (q)	3.66 (q) [a]	1.36 (t), 1.23 (t)

[a] $^4J_{F-H}$ = 5 Hz.

The ^{13}C-NMR data are in accord with the structures of *(2)* and *(3)* (Table 2). Relative to *(1)* and *(3)* the positive charge leads to a paramagnetic shift of the carbyne carbon atom of *(2)* but to an upfield shift of the carbonyl ligands. The absence of splitting of the NEt_2 signals indicates a linear arrangement of the Cr—C(carbyne)—N system. The signal of the carbene carbon in *(3)* is split into a doublet by interaction with the fluorine atom; further F—C coupling occurs with the *cis* orientated CO groups and the *Z*-NCH_2 group.

Table 2. ^{13}C-NMR spectra of complexes *(2)* and *(3)* in CD_2Cl_2 at −30 °C; values in ppm relative to CD_2Cl_2 = 54.16 ppm.

	Cr-C	CO_{cis}	CO_{trans}	NCH_2 (*E*)	NCH_2 (*Z*)	NCH_2CH_3 (*E*,*Z*)
(2)	282.22	207.68	201.85	49.63		13.70
(3)	245.70 [a]	216.52 [b]	221.48	49.30	43.85 [c]	14.35, 13.70

[a] $^1J_{F-C}$ = 393.1 Hz; [b] $^3J_{F-C}$ = 9.8 Hz; [c] $^3J_{F-C}$ = 17.1 Hz.

In its ^{19}F-NMR spectrum (δ values relative to CF_3COOH), compound *(2)* only shows one sharp signal at −73.13 ppm for the tetrahedral anion $[BF_4]^-$ as expected. *(3)* displays a triplet at 152.30 ppm which is due to coupling ($^4J_{F-H}$ = 5 Hz) with the *Z*-NCH_2 group.

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The linear conductivity-concentration relationship observed in highly dilute solutions of *(2)* underlines the saltlike character of the carbyne complex.

In contrast to the analogous chlorocarbene complex[2], the fluorocarbene complex *(3)* is very stable. The chlorocarbene complex gives *trans*-chloro(tetracarbonyl)diethylaminocarbynechromium in CH_2Cl_2 solution at temperatures up to 30 °C, and pentacarbonyl(ethyl isocyanide)chromium is formed at 35—40 °C. No comparable reactions of *(3)* were observed under similar conditions.

Procedure:

All operations should be performed under N_2 and with dried, N_2-saturated solvents.

On passage of BF_3 into a solution of *(1)* (1.6 g, 5 mmol) in CH_2Cl_2 (50 ml) at −100 °C, the initially yellow solution turns red. After warming up to −30 °C the solution is evaporated to dryness and the red residue repeatedly washed with ether. For further purification the substance is dissolved in CH_2Cl_2 and transferred onto a cooled frit filled with silica gel. After washing out impurities with CH_2Cl_2 and ether, compound *(2)* is eluted with methanol and recrystallized from CH_2Cl_2/Et_2O. Yield: 1.45 g (80 %).

A solution of $[N(C_4H_9)_4]F$ (1.31 g, 5 mmol) in THF (20 ml) is added dropwise to a solution of *(2)* (1.82 g, 5 mmol) in CH_2Cl_2 (20 ml) at −78 °C, the color changes from red to yellow. After 0.5 h the solvent mixture is drawn off and the residue chromatographed on silica gel with CH_2Cl_2 at −20 °C. The yellow zone contains the desired product *(3)*, which is recrystallized from ether/pentane. Yield: 0.9 g (61 %).

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CAS Registry numbers:
(1), 28471-37-6; *(2)*, 60525-61-3; *(3)*, 60525-64-6; $[N(C_4H_9)_4]F$, 429-41-4; ^{13}C, 14762-74-4

[1] Transition metal-carbene complexes, Part 94.—Part 93: *E. O. Fischer, W. Held, F. R. Kreissl, A. Frank*, and *G. Huttner*, Chem. Ber., in press.
[2] *E. O. Fischer, W. Kleine*, and *F. R. Kreissl*, J. Organomet. Chem. *107*, C 23 (1976).
[3] *E. O. Fischer* and *H. J. Kollmeier*, Angew. Chem. *82*, 325 (1970); Angew. Chem. Int. Ed. Engl. *9*, 309 (1970).
[4] *E. Moser* and *E. O. Fischer*, J. Organomet. Chem. *13*, 387 (1968); *E. O. Fischer, F. R. Kreissl, E. Winkler*, and *C. G. Kreiter*, Chem. Ber. *105*, 588 (1972).

Reactions of Arenetricarbonylchromium Complexes with Nitrosyl Chloride[**]

By *Max Herberhold* and *Wolfgang Bernhagen*[*]

According to investigations by *Connelly et al.*[1,2] complexes of the type $(ar)Cr(CO)_3$ *(1)* react with nitrosyl hexafluorophosphate (in methanol/toluene, nitromethane or liquid sulfur dioxide) *via* substitution of one CO ligand to give yellow, air-stable salts:

$$(ar)Cr(CO)_3 + NO^+PF_6^- \rightarrow [(ar)Cr(CO)_2NO]^+PF_6^- + CO$$
(1) *(2)*

ar = $C_6H_nMe_{6-n}$ (n = 3-6)

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We found that the corresponding reaction with nitrosyl chloride (in tetrahydrofuran or methylene dichloride) at room temperature leads to complete decarbonylation of *(1)*; attempted characterization of the paramagnetic, NO-containing products (ν(N≡O) 1852 and 1710 cm^{-1} resp.) has so far met without success. However, below −30 °C intense red solutions are formed which contain reactive complex fragments of the type $[CrCl(CO)_2NO]$ *(3)* as main component:

$$(ar)Cr(CO)_3 + ClNO \xrightarrow[-30\,^\circ C]{(THF)} [CrCl(CO)_2NO] + ar + CO$$
(1) *(3)*

ar = benzene, mesitylene, hexamethylbenzene, cycloheptatriene, *p*-substituted toluene X-C_6H_4-Me (X = F, OMe, NMe_2)

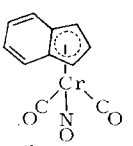
The composition and preparative significance of the—presumably solvent-stabilized—complex fragment *(3)* is shown by the following results:

1. IR spectra of THF solutions of *(3)* at −30 °C always show the same absorptions for a dicarbonylnitrosyl grouping (ν(C≡O) 2024 and 1942, ν(N≡O) 1681 cm^{-1}); the frequencies do not depend on the nature of the starting complex *(1)*. This means that the π-bonded arene ligand (ar) is cleaved from the metal on reaction of *(1)* with ClNO. On warming the solution to +20 °C the $Cr(CO)_2NO$ absorptions disappear; at the same time CO is liberated[3].

2. Addition of solid cyclopentadienylsodium to the red THF solution of *(3)* affords the well-known orange-red complex $CpCr(CO)_2NO$ *(4a)*[4] in about 40 % yield:

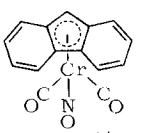
$$[CrCl(CO)_2NO] + CpNa \xrightarrow{(THF)} CpCr(CO)_2NO + NaCl$$
(3) *(4a)*

Analogous reactions with solutions of indenyl- and fluorenyllithium lead to the novel complexes *(4b)* and *(4c)*, respectively, in about 20—40 % yields:



(4b)

ν(C≡O) 2019, 1946
ν(N≡O) 1699 cm^{-1} (benzene)



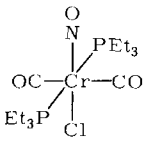
(4c)

ν(C≡O) 2014, 1942
ν(N≡O) 1697 cm^{-1} (benzene)

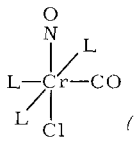
In both cases a *pentahapto*-coordination of the π-bonded ligand is to be assumed, as has also been postulated for the isoelectronic indenyl- and fluorenyltricarbonylmanganese complexes[5].

3. On reaction of the red THF solution of *(3)* with two-electron ligands (L) containing N or P, diamagnetic complexes are obtained which derive from a so far unknown parent compound *trans*-$[CrCl(CO)_4NO]$. Reaction with pyridine (py) affords the adduct $CrCl(CO)_2(py)_2NO$ *(5)* containing the CO-ligands in *cis* position. Similar products with *cis*-dicarbonyl grouping are also formed with bidentate chelate ligands such as 2,2'-bipyridyl (bpy) or ethylenebis(diphenylphosphane) (diphos).

In contrast, reaction of the THF solution of *(3)* with monodentate P-containing ligands leads to either *trans*-dicarbonyl or monocarbonyl complexes. In the case of the yellow complex containing triethylphosphane, $CrCl(CO)_2(PEt_3)_2NO$ *(6)*, both the CO and the PEt_3 ligands must be *trans* to each other (C_{2v} symmetry) on the basis of the IR spectrum (ν(C≡O) 1949 cm^{-1}) (Table 1) and the ^{31}P-NMR spectrum (singlet at δ = 35.02 ppm[6]), cf. ref.[7].



(6)



(7a), L = PMe_3
(7b), L = PMe_2Ph
(7c), L = $P(OMe)_3$

On reaction with an excess of trimethylphosphane, dimethylphenylphosphane or trimethylphosphite, compounds of the type *mer*-$[CrCl(CO)L_3(NO)]$ (7) are obtained. The meridial configuration follows from the ^{31}P-NMR spectrum[6], which shows an AB_2 pattern (*e.g.* (7c): $\delta(A) = 166.5$, $\delta(B) = 173.3$ ppm; $J_{AB} = 89$ Hz); of the three alternative structural possibilities that with Cl and NO ligands *trans* to each other is expected to be preferred.

Table 1. Characteristic IR-absorptions (in THF solution).

Complex	Color	ν(C≡O) [cm^{-1}]	ν(N≡O) [cm^{-1}]
$CrCl(CO)_2(py)_2NO$ (5)	yellow	2033 1955	1669
$CrCl(CO)_2(bpy)NO$	red-brown	2033 1951	1684 [a]
$CrCl(CO)_2$(diphos)NO	brown-yellow	2029 1968	1676
$CrCl(CO)_2(PEt_3)_2NO$ (6)	yellow	1949	1658
$CrCl(CO)(PMe_3)_3NO$ (7a)	brown-yellow	1921	1627
$CrCl(CO)(PMe_2Ph)_3NO$ (7b)	orange-yellow	1922	1627
$CrCl(CO)[P(OMe)_3]_3NO$ (7c)	yellow	1969	1662

[a] The band is split.

Experimental[8]

A solution of ClNO (6 ml, 3.24 mmol) in THF is added dropwise to a solution of (mesitylene)$CrCO_3$ (0.93 g, 3.63 mmol) in THF (60 ml) at −78 °C; evolution of gas and red coloration of the solution indicate formation of the reactive intermediate (3).

Dicarbonyl(indenyl)nitrosylchromium (4b): To the THF solution of (3) at −78 °C is added a solution of indenyllithium (7 mmol) (prepared from indene and CH_3Li in Et_2O at −30 °C). After thawing, the reaction mixture is stirred for 2 h at room temperature, filtered, the filtrate evaporated to dryness and the resulting residue (4b) extracted with pentane and purified by both chromatography (Al_2O_3/pentane) and double recrystallization from pentane. Red-gold platelets, m.p. 41—42 °C (under N_2); yield 0.28 g (34.1 %).

Carbonylchloronitrosyl[mer-tris(trimethyl phosphite)]chromium (7c): To the THF solution of (3) at −78 °C is added 2 ml (16.9 mmol) $P(OMe)_3$ and the mixture stirred without cooling for *ca.* 10 h. (7c) is extracted from the residue of the filtered reaction solution with CH_2Cl_2 and purified by chromatography (Al_2O_3/CH_2Cl_2). Yellow crystals from CH_2Cl_2/pentane (−78 °C), m.p. 81 °C (under N_2); yield 0.51 g (30.1 %).

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CAS Registry numbers:
(1) (ar = benzene), 1202-08-5; (1) (ar = mesitylene), 12129-67-8; (1) (ar = hexamethylbenzene), 12088-11-8; (1) (ar = cycloheptatriene), 12125-72-3; (1) (ar = F-C_6H_4-*p*-Me), 12116-25-4; (1) (Ar = MeO-C_6H_4-*p*-Me), 12109-02-3; (1) (ar = Me_2N-C_6H_4-*p*-Me), 12247-19-7; (3), 60260-20-0; (4b), 60260-19-7; (4c), 60260-18-6; (5), 60260-14-2; (6), 60260-35-7; (7a), 60260-36-8; (7b), 60260-37-9; (7c), 60260-38-0; $CrCl(CO)_2$(bpy)NO, 60260-39-1; $CrCl(CO)_2$(diphos)NO, 60260-40-4; indenyllithium, 20669-47-0; *trans*-$[CrCl(CO)_4NO]$, 60260-41-5; ClNO, 2696-92-6; CpNa, 4984-82-1

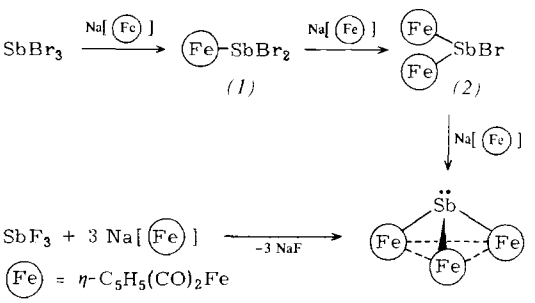
[1] *D. E. Ball* and *N. G. Connelly*, J. Organomet. Chem. *55*, C24 (1973); *N. G. Connelly* and *R. L. Kelly*, J. Chem. Soc. Dalton *1974*, 2334.
[2] *N. G. Connelly*, *Z. Demidowicz*, and *R. L. Kelly*, J. Chem. Soc. Dalton *1975*, 2335.
[3] A further strong absorption at 1708 cm^{-1}, which is not affected on warming the sample to room temperature, can be assigned to a secondary product free of CO.
[4] *E. O. Fischer*, *O. Beckert*, *W. Hafner*, and *H. O. Stahl*, Z. Naturforsch. *10b*, 598 (1955).
[5] *R. B. King* and *A. Efraty*, J. Organomet. Chem. *23*, 527 (1970).
[6] Bruker HFX-90 ([D_6]-acetone, ref. 85 % H_3PO_4); measurements by Dr. *C. G. Kreiter*.
[7] A recent article (*N. G. Connelly*, *B. A. Kelly*, *R. L. Kelly*, and *P. Woodward*, J. Chem. Soc. Dalton *1976*, 699) describes analogous complexes of the type *trans*-$[CrX(CO)_2L_2(NO)]$ (X = I; L = PPh_3, $PMePh_2$, PMe_2Ph, $P(OPh)_3$), which can be obtained by reaction of $[(ar)Cr(CO)_2NO]PF_6$ (2) with halides X^- and subsequent reaction with phosphanes L.
[8] All operations carried out under N_2.

Tris[dicarbonyl(η-cyclopentadienyl)ferrio]stibane—A 5B-Element Base with Total Transition-Metal Substitution[1]

By *Wolfgang Malisch* and *Peter Panster*[*]

Contrary to earlier assumptions[2], simple transition-metal substituted 5B-element derivatives of the type $L_nM—ER_2$ (E = P, As, Sb) are frequently capable of existing in substance[1,3] and exhibit increasing stability towards aggregation and elimination processes along the series phosphorus, arsenic, antimony[1,4]. Permetalation therefore seems possible, especially in the case of the higher homologs. Previously it could be demonstrated in three cases, but only with products in which the M_3E group is integrated in a specific cluster system[5].

We have now been able to synthesize for the first time a permetalated 5B-element base of the usual bonding type by heterogeneous reaction of $SbBr_3$ or SbF_3 with $Na[Fe(CO)_2(C_5H_5)]$.



(3), black-brown needles, 165-167 °C (dec.)

Whereas the mono- and dimetalated intermediates are also isolable by use of $SbBr_3$ (in cyclohexane)[6], halogen/transition-metal exchange starting with SbF_3 (in benzene) immediately leads to (3), in spite of the stoichiometry. Both methods afford the surprisingly thermostable permetalated stibane together with the dinuclear complex $[\eta\text{-}C_5H_5(CO)_2Fe]_2$, which can be formed in the synthesis both by attack of the nucleophile $[\eta\text{-}C_5H_5(CO)_2Fe]^-$ at an already coupled Fe—Sb bond as well as by subsequent decomposition of (3). The tendency to undergo elimination is chiefly observed in polar media such as tetrahydrofuran; on dissolution in halogenated solvents spontaneous decomposition takes place.

Supporting evidence for the proposed constitution of (3) is provided by the stepwise metalation of $SbBr_3$ and by the readiness of (3) to add coordinatively to a complex fragment with preservation of its bonding skeleton:

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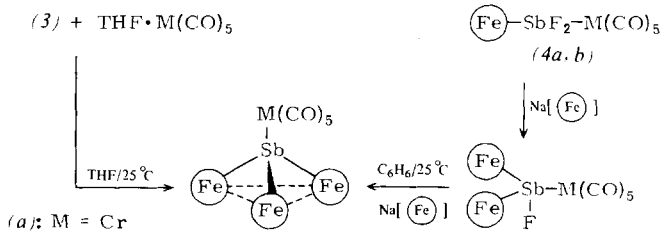

Because of its sensitivity towards solvolysis this reaction of *(3)* gives, despite mild conditions, only moderate yields (35 and 32 %, resp.) of *(6a)* and *(6b)*, so the more favorable route for the synthesis of *(6)* is "transition-metal metalation" of the SbF_2-bridged dinuclear complexes *(4a)* and *(4b)*[7]. The fluoride/metalate exchange also proceeds extremely rapidly at bridging Sb-atoms, but, in contrast to the metalation of SbF_3, a directed synthesis of intermediates, *e.g. (5a)* is also possible. *(6a)* and *(6b)* are examples of a bonding type in which all valence electrons of the 5B-element atom are used for bonding to transition metal atoms. Both complexes decompose on melting with evolution of $M(CO)_6$; the degradation with elimination of $[\eta\text{-}C_5H_5(CO)_2Fe]_2$ is only of secondary importance. The coordinate requirement of the lone pair of electrons accordingly effects stabilization of the ferriostibane moiety, but at the same time promotes lability of the CO ligand in the $Cp(CO)_2Fe$ grouping.

Table 1. ^{1}H-NMR [a] and IR data [b] of the antimony transition-metal complexes *(3)*, *(5a)*, *(6a)*, and *(6b)* [c].

	$\delta_{C_5H_5}$ [ppm]	ν_{CO} [cm^{-1}]								δ_F [ppm] [d]
(3)	4.55 (s)	2017 vs	1985 s	1979 sh	1971 m	1944 vs				
(5a)	4.50 (s)	2054 m	2021 s	2007 s	1981 s	1965 s	1935 sh	1926 vs, br		233
(6a)	4.77 (s)	2042 s	2008 vs	1994 vs	1988 sh	1964 m	1951 m	1914 vs, br		
(6b)	4.73 (s)	2052 s	2010 s	1994 vs	1987 sh	1964 m	1950 m	1914 vs	1900 sh	

[a] C_6D_6; values rel. TMS int.
[b] 0.1 mm NaCl-liquid cuvettes: *(3)* C_6H_{12}; *(5a)*, *(6a)*, *(6b)* THF.
[c] Analytical data in agreement with the given formula.
[d] THF; values at higher field w.r.t. $CFCl_3$ ext.

The IR spectra reveal a high σ-donor/π-acceptor ratio for the novel ligand system *(3)* $[A_1^{(2)}(M(CO)_5)$: 2042 cm^{-1} (Cr), 2052 cm^{-1} (W)], mainly as a result of the pronounced electron-donor properties of the metal substituents.

Experimental:

Tris[dicarbonyl(η-cyclopentadienyl)ferrio]stibane (3):

$Na[Fe(CO)_2(C_5H_5)]$ (0.30 g, 1.50 mmol) and *(2)* (0.78 g, 1.40 mmol) are combined in 80 ml cyclohexane; the heterogeneous reaction mixture is stirred at room temperature for 55 h. The solution is warmed briefly to 60—70 °C and filtered; on cooling, *(3)* slowly crystallizes. The crystals are filtered off, washed three times with 15 ml ether (40 °C), and finally dried in a vacuum. Yield 0.61 g (66.8 %).

Pentacarbonyl{tris[dicarbonyl(η-cyclopentadienyl)-ferrio]-stibane}chromium(0) (6a):

(4a) (0.53 g) (1.00 mmol) is allowed to react with $Na[Fe(CO)_2(C_5H_5)]$ (0.40 g, 2.00 mmol) in benzene (40 ml) for 2 days at 25 °C. The solution is concentrated to 20 ml, heated to boiling and filtered. The pure, quadrinuclear complex *(6a)* is isolable from the filtrate after two recrystallizations from benzene. Yield: 0.47 g (68.3 %).

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CAS Chemistry numbers:
(1), 34822-16-9; *(2)*, 59090-85-6; *(3)*, 60260-25-5; *(4a)*, 60260-24-4; *(4b)*, 60260-23-3; *(5a)*, 60260-22-2; *(6a)*, 60260-21-1; *(6b)*, 60270-31-7; $SbBr_3$, 7789-61-9; $Na[\eta\text{-}C_5H_5(CO)_2Fe]$, 12152-20-4; SbF_3, 7783-56-4; THF $Cr(CO)_5$, 15038-41-2; THF $W(CO)_5$, 36477-75-5

[1] Transition-Metal Substituted 5B-Element Systems, Part 13. This work was supported by the Deutsche Forschungsgemeinschaft. Part 12: *W. Malisch, P. Panster,* and *R. Alsmann,* Z. Naturforsch., in press.
[2] *R. G. Hayter,* Inorg. Chem. *2*, 1031 (1963).
[3] *W. Malisch* and *M. Kuhn,* Angew. Chem. *86*, 51 (1974); Angew. Chem. Int. Ed. Engl. *13*, 85 (1974); *W. Malisch* and *P. Panster,* J. Organomet. Chem. *99*, 421 (1975); Chem. Ber. *108*, 700 (1975).
[4] Cf. *W. Malisch* and *P. Panster,* VII. Int. Conf. Organomet. Chem., Venice 1975, Abstr. Pap., p. 174.
[5] *A. S. Foust* and *L. F. Dahl,* J. Am. Chem. Soc. *92*, 7337 (1970); *A. Vizi-Orosz, V. Galamb, G. Palyi, L. Marko, G. Bor,* and *G. Natile,* J. Organomet. Chem. *107*, 235 (1976); *A. Vizi-Orosz, ibid. 111*, 61 (1976).
[6] *P. Panster* and *W. Malisch,* Chem. Ber. *109*, 692 (1976).
[7] *P. Panster* and *W. Malisch,* Chem. Ber. *109*, 2112 (1976).

Cyclization Reactions at Electropositive Silicon[**]

By *Uwe Klingebiel* and *Anton Meller*[*]

We were recently able to show that incorporation of bulky substituents into monoalkylaminofluorosilanes[1, 2] led, in the cyclization reaction with butyllithium with loss of lithium fluoride and butane, to suppression of dimerization in favor of a nucleophilic rearrangement at the positively charged silicon[3].

A slight variation (diminution) in the size of the substituent groups on the central silicon atom of such monoalkylaminofluorosilanes, *e.g.* in *(1)*, leads under comparable reaction conditions—as we have now shown—to another type of cyclization process in silicon chemistry[4]: Because of the high reactivity of the silicenium intermediate, in intact monoalkylamino groups a proton is removed from a methylsilylamino group with ring closure to *(3)* and formation of butane.

In contrast the aminofluorosilane *(2)*, which is bulkier than *(1)*, once again reacts in the usual way[3], with migration of a methanide ion and ring closure to *(4)*; this, together with the formation of butane with the hydrogen atom of the monoalkylamino group provides evidence for the occurrence of silicenium ylide[3].

On changing the reaction conditions (solvent, temperature) expected transitions between the three types of cyclization depending on the substituents R are observed[5]. In the rearrangement reactions the corresponding *n*-butyl substituted cyclobutane could also be isolated as by-product.

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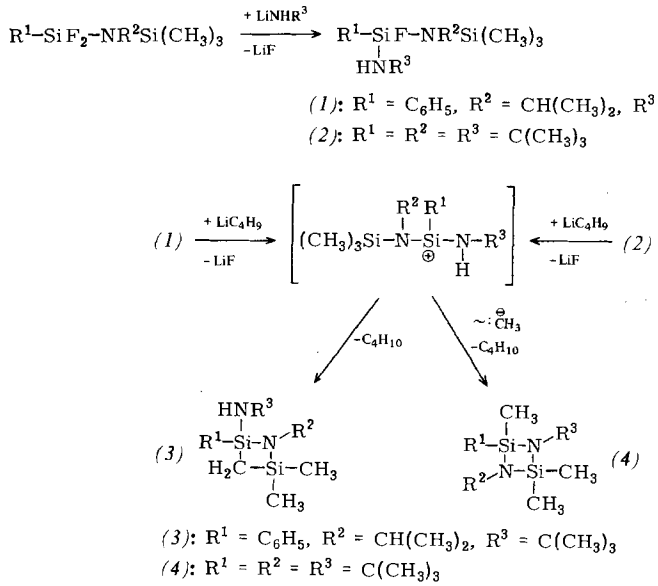

tert-Butylaminoisopropyl(trimethylsilyl)aminofluorophenylsilane (1):
Yield 90 %; b.p. 63 °C/0.01 torr; MS (70 eV): $m/e = 326$ (rel. int. 26 %, M^+); IR: 3400 cm^{-1} (νNH); ^{1}H-NMR: 0.17 [Me_3Si, $J_{HF} = 0.4$ Hz], 1.21 [Me_2C, $J_{HF} = 1.2$ Hz], 1.24 [Me_3C, $J_{HF} = 0.3$ Hz], 3.45 [CH, $J_{HF} = 2.0$ Hz], 7.6 ppm [C_6H_5].

tert-Butylamino-tert-butyl(trimethylsilyl)amino-tert-butylfluorosilane (2):
Yield 75 %; b.p. 66 °C/0.01 torr; MS (70 eV): $m/e = 320$ (1 %, M^+); IR: 3400 cm^{-1} (νNH); ^{1}H-NMR: 0.30 [Me_3Si], 0.89 [Me_3C, $J_{HF} = 1.3$ Hz], 1.26 [Me_3CNH, $J_{HF} = 0.6$ Hz], 1.43 ppm [Me_3CNSi, $J_{HF} = 0.5$ Hz]; ^{19}F-NMR: −32.5 ppm.

1-Isopropyl-2-dimethyl-4-tert-butylamino-4-phenyl-1-aza-2,4-disilacyclobutane (3):
Yield 70 %; b.p. 69 °C/0.01 torr; MS (70 eV): $m/e = 306$ (8 %, M^+); IR: 3400 cm^{-1} (νNH); ^{1}H-NMR: 0.28, 0.34 [MeSi], 0.39 [CH_2Si_2], 1.08 [Me_2C], 1.32 [Me_3C], 1.5 [NH], 3.37 [CH], 7.48 ppm [C_6H_5].

1,3-Bis(tert-butyl)-2-dimethyl-4-tert-butyl-4-methyl-1,3-diaza-2,4-disilacyclobutane (4):
Yield 75 %; m.p. 102 °C; MS (70 eV): $m/e = 300$ (1 %, M^+); ^{1}H-NMR: 0.32, 0.35 [MeSi], 1.08 [Me_3CSi], 1.20 ppm [Me_3CN].

^{1}H-NMR spectra: 30 % solution in CH_2Cl_2, TMS int.
^{19}F-NMR spectra: 30 % solution in CH_2Cl_2, C_6F_6 int.
Elemental analysis gave correct results for all compounds.

Experimental:

C_4H_9Li (0.11 mol, 15 % solution in hexane) is added dropwise with stirring at room temperature to 0.1 mol monoalkylaminofluorosilane [*(1)*, *(2)*]. LiF and C_4H_{10} split off in an exothermic reaction. For completion of reaction the mixture is heated to boiling for 12 h. After removal of hexane the heterocyclic products are distilled in a vacuum [*(3)*] or sublimed [*(4)*].

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CAS Registry numbers:
(1), 60253-73-8; *(2)*, 60253-74-9; *(3)*, 60253-75-0; *(4)*, 60253-76-1; $C_6H_5SiF_2NCH(CH_3)_2Si(CH_3)_3$, 60253-77-2; $C(CH_3)_3SiF_2NC(CH_3)_3Si(CH_3)_3$, 60253-78-3; $LiNHC(CH_3)_3$, 37828-549

[1] *U. Klingebiel* and *A. Meller*, Chem. Ber. *109*, 2430 (1976).
[2] *U. Klingebiel* and *A. Meller*, Z. Anorg. Allg. Chem., in press.
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Bis(tri-*tert*-butylsilyl)cadmium: The First Silylcadmium Compound Isolated in Substance[**]

By *Lutz Rösch* and *Hartwig Müller*[*]

Previous investigations[1] on the synthesis of silylmetal compounds according to

$$n\ R_3SiH + R'_nM \longrightarrow (R_3Si)_nM + n\ R'H$$

R = Et, Ph; R' = Et, Ph, *t*Bu;
M = main group metal

have shown that this "hydride reaction" proceeds in the expected manner only under drastic conditions. The main drawback of this method was that many of the silylmetal compounds thus synthesized could not be isolated from the reaction mixture but only their existence demonstrated on the basis of secondary reactions—*e.g.* also in the case of the only previously known organosilylcadmium compound, bis(triethylsilyl)cadmium[2].

Should in fact a hydride transfer be the determining factor in the course of the reaction then polarization of the silane hydrogen is of decisive importance; consequently, tri-*tert*-butylsilane[3] [low Si—H stretching frequency at 2080 cm^{-1}, small $^1J(^1H\text{-}^{29}Si)$ coupling constant of 179.7 Hz and chemical shift of 3.39 ppm rel. TMS] ought to be a particularly effective silylating reagent.

We have found that tri-*tert*-butylsilane *(1)* reacts with diethylcadmium *(2)* in the molecular ratio 2:1 with loss of ethane already at 90 °C:

$$2\ (t\text{-}C_4H_9)_3SiH + (C_2H_5)_2Cd \longrightarrow [(t\text{-}C_4H_9)_3Si]_2Cd + 2\ C_2H_6$$
(1) *(2)* *(3)*

As reaction proceeds the liquid mixture of *(1)* and *(2)* gradually solidifies; colorless crystals are formed, which after purification by recrystallization from benzene can be identified by spectroscopic investigation and elemental analysis as bis(tri-*tert*-butylsilyl)cadmium *(3)*.

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The ^{1}H-NMR spectrum (60 MHz; rel. C_6H_6 int.) of *(3)* shows only one signal at 1.33 ppm (converted to TMS), which expectedly exhibits no coupling with cadmium (^{111}Cd, $I=1/2$, rel. abundance 12.86%; ^{113}Cd, $I=1/2$, rel. abundance 12.34%). In contrast the ^{13}C-NMR spectrum (20 MHz; rel. C_6D_6 int.) shows two signals at 95.06 and 102.58 ppm, both flanked by coupling satellites [$^2J(^{13}C\text{-}^{111/113}Cd)=31$ Hz, $^3J(^{13}C\text{-}^{111/113}Cd)=11.4$ Hz]. No Si—H stretching vibrations are observed in the IR spectrum (solution in Nujol, CsI disks).

Experimental:

All operations were carried out under an atmosphere of dry oxygen-free argon. The starting compounds *(1)* and *(2)* were prepared by known methods[4]. *(1)* (7.5 mmol) and *(2)* (3.75 mmol) were transferred to a 25 ml flask furnished with an argon inlet and a reflux condenser connected to a gas burette *via* a bubbler. On heating to 90°C, 156 ml gas was evolved within 24 h (IR: C_2H_6; *ca.* 86%). Unconsumed *(1)* could be removed at 60°C/2.5×10^{-5} mbar. The crude product was purified by recrystallization from benzene. *(3)* was obtained as pale yellow crystals m.p. *ca.* 140°C (decomp.) which turned green-black on exposure to air and moisture.

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CAS Registry numbers:
(1), 18159-55-2; *(2)*, 592-02-9; *(3)*, 60349-27-1; ^{13}C, 14762-74-4

[1] *N. S. Vyazankin*, Organomet. Chem. Rev. *A3*, 323 (1968); *N. S. Vyazankin, E. N. Gladyshev, S. P. Korneva, G. A. Razuvaev*, and *E. A. Arkhangel'skaya*, Zh. Obshch. Khim. *38*, 1803 (1968); *R. A. Jackson*, Chem. Commun. *1966*, 827.

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Carbanion Complexes of Nickel(0)

By *Klaus Jonas, Klaus Richard Pörschke, Carl Krüger*, and *Yi-Hung Tsay*[*]

Transition-metal(0) compounds in which simple carbanions such as CH_3^- or $C_2H_5^-$ are coordinated as electron donors to the metal atom were, to our knowledge, previously unknown[1,2]. We report here on novel nickel(0) complexes in which such a σ-M^0—C bonding is present.

During investigations on alkali metal compounds of nickel[3] we found that reaction of binary Ni^0-olefin complexes such as (CDT)Ni or $(COD)_2Ni$[4] with organolithium compounds LiR (Ni/LiR = 1:1) and ethylene in the presence of strong n-donor ligands such as tetrahydrofuran or *N,N,N',N'*-tetramethylethylenediamine leads to complexes in which two ethylene molecules besides a carbanion ligand R^- are bonded to a nickel atom with formation of a $R\text{—}Ni^0(C_2H_4)_2$ anion.

$$(COD)_2Ni + LiR + 2\ C_2H_4 + 2\ (CH_3)_2N\text{—}CH_2CH_2\text{—}N(CH_3)_2 \xrightarrow[-2\ COD]{Et_2O}$$

$$\left[Li\left\{(CH_3)_2NCH_2CH_2N(CH_3)_2\right\}_2\right]^{\oplus}\left[R\text{—}Ni(C_2H_4)_2\right]^{\ominus}$$

(1a), R = CH_3
(1b), R = C_2H_5
(1c), R = C_6H_5

COD = 1,5-cyclooctadiene

The complexes *(1)* are characterized by elemental analysis and ^{1}H-NMR data, as well as by reaction with ethanol or carbon monoxide. With ethanol two equivalents of diamine are liberated per equivalent of Li; the ethyl compound *(1b)* yields the calculated amount of ethylene and ethane, while the methyl compound *(1a)* yields also the calculated amount of methane together with ethylene and ethane (from ethylene). On the other hand, the ethylene moiety in *(1a)*, *(1b)* and *(1c)* can also be displaced quantitatively (as C_2H_4) by carbon monoxide.

In the ^{1}H-NMR spectrum of *(1)* (in [D_8]-THF) the signals of the amine protons are not shifted compared to free amine; it thus follows that the amine ligands initially coordinated to the lithium are completely displaced by [D_8]-THF. In all three cases singlets are found for the protons of the ethylene ligands coordinated to nickel, for *(1a)* at $\tau=8.26$, *(1b)* at $\tau=8.42$ and for *(1c)* at $\tau=8.34$. The signals of the phenyl protons in *(1c)* appear at $\tau=2.4$ and 3.4 (intensity ratio 2:3). The methyl protons in *(1a)* are observed as a singlet at $\tau=10.58$, while the ethyl compound *(1b)* shows a triplet for the methyl protons at $\tau=8.76$ and a quartet for the methylene protons at $\tau=9.42$ with $J=7.5$ Hz. All ^{1}H-NMR spectra are essentially temperature-independent in the range −80°C to +20°C. Exchange between complexed and added free ethylene is not observed.

The specific conductivities of complexes *(1)* are $1\text{—}2\times10^{-3}$ Ω^{-1} cm^{-1} (0.25 M in THF at −30°C), and thus correspond closely to the value quoted for $LiClO_4$ in THF; hence the compounds are obviously largely ionic. Also in agreement with this is the result of X-ray structure analysis, according to which *(1a)* is composed of separated $Li[(CH_3)_2NCH_2CH_2N(CH_3)_2]_2$ cations and $CH_3Ni(C_2H_4)_2$ anions in the crystalline state.

Crystal data [*(1a)*][5]: $a=10.022(2)$, $b=16.121(3)$, $c=14.501(1)$ Å; $\beta=96.82(1)°$; space group $P2_1/n$, $Z=4$; 3395 reflections, 1694 of which are considered unobserved; $R=0.069$.

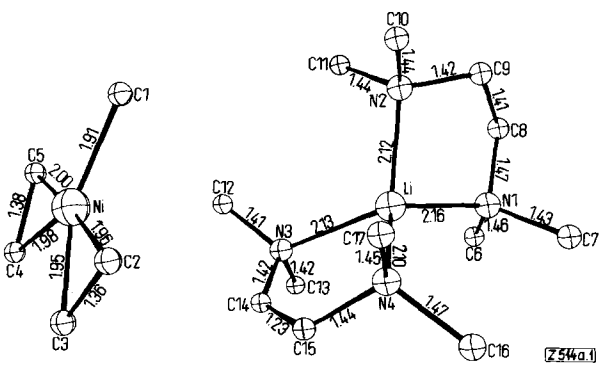

Fig. 1. Crystal structure of the carbanion complex *(1a)*.

In *(1a)* the two ethylene molecules together with the methyl group are oriented exactly trigonal-planar about the nickel atom (Fig. 1). The Ni—C1 σ-bond with a value of 1.91 Å is unusually short[6]. The short C=C bond lengths in the ethylene indicate only weak bonding to the nickel. The two diamine ligands surround the lithium cation tetrahedrally. In the solid state the complex is one-dimensionally polymeric; each lithium cation is situated equidistant between two Ni—CH_3 units (Li—Cl* 5.351 and 5.390 Å; Li—Ni* 5.777 and 5.800 Å).

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[**] X-ray structure analysis.

Experimental:

A mixture of $(COD)_2Ni$[4] (6.36 g, 23.1 mmol) and *N,N,N',N'*-tetramethylethylenediamine (20 ml) in ether (80 ml) is saturated with ethylene at −20 °C. A solution of $LiCH_3$ (24 mmol) in ether [from $Hg(CH_3)_2$ and Li in $(C_2H_5)_2O$] is then added and the mixture stirred and allowed to warm to room temperature. A clear, yellow solution is obtained. On re-cooling to −60 °C *(1a)* crystallizes out (yield 7.6 g, 89 %). *(1a)* and *(1c)* are stable under argon at room temperature.

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CAS Registry numbers:
(1a), 60349-34-0; *(1b)*, 60384-04-5; *(1c)*, 60349-37-3; $(COD)_2Ni$, 1295-35-8

[1] *P. J. Davidson, M. F. Lappert,* and *R. Pears,* Chem. Rev. 76, 219 (1976).
[2] *R. R. Schrock* and *G. G. Parshall,* Chem. Rev. 76, 243 (1976).
[3] *K. Jonas,* Angew. Chem. *88*, 51 (1976); *87*, 809 (1975); Angew. Chem. Int. Ed. Engl. *15*, 47 (1976); *14*, 752 (1975).
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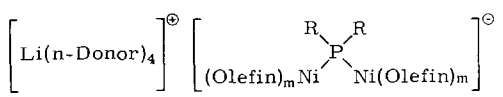
[6] *P. Binger, M. J. Doyle, C. Krüger,* and *Y.-H. Tsay,* Transition Met. Chem., in press.

The Anion PR_2^- as Single Bridge between Two Nickel(0) Coordination Centers

By *Klaus Jonas* and *Ludwig Schieferstein*[*]

The previously known transition-metal complexes with phosphido bridges contain almost without exception relatively tightly bound groups such as CO, PR_3 or η^5-C_5H_5 as further ligands[1], thus making ligand exchange reactions relatively difficult. The observation that treatment of organolithium compounds with ethylene leads to formation of stable carbanion-nickel(0) complexes[2] gave us cause to investigate also the reactivity of lithium diorganylphosphides towards nickel(0)-olefin complexes. In contrast to the carbanion, the anion PR_2^- should be able to bind two Ni^0-olefin moieties *via* the two donor orbitals of the phosphorus to give an ionic multimetal system *(1)* containing two neighboring nickel atoms and easily displaceable olefin ligands.



(1)

We have found that reaction of $(COD)_2Ni$[4] with $LiPR_2$[3] ($Ni/LiPR_2 = 2:1$) and ethylene leads to complexes of type *(1)* in high yields.

$$2\ (COD)_2Ni + LiPR_2 + 4\ C_2H_4 \xrightarrow[-30\,°C\ \text{bis}\ 0\,°C]{THF} (1) + 4\ COD$$

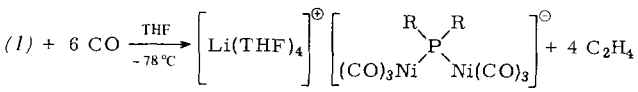
(1a), R = C_6H_{11}, n-Donor = THF, Olefin = C_2H_4, m = 2

(1b), R = C_6H_5, n-Donor = THF, Olefin = C_2H_4, m = 2

COD = 1.5-cyclooctadiene

The novel compounds *(1a)* and *(1b)* are characterized by complete elemental analysis and ^{1}H-NMR spectra. For both complexes the spectra show only a narrow, slightly split (evidently by ^{31}P-coupling) signal at $\tau = 7.7$ for all 16 ethylene protons, even at −80 °C. Unlike *(1a)*, for *(1b)* exchange between complexed and added free ethylene is observed.

As displacement experiments have already shown, the bound ethylene in *(1)* can be readily replaced quantitatively by other olefins such as butadiene, as well as by carbon monoxide, with complete retention of the anionic R_2PNi_2-moiety. Thus, on reaction with CO the previously unknown carbonyl complexes *(2)* are formed, which are characterized by elemental



(2a), R = C_6H_{11}, ν_{CO} in THF: 2030 (w), 2006 (s), 1945 cm^{-1} (br, vs)

(2b), R = C_6H_5, ν_{CO} in THF: 2039 (s), 2019 (s), 1960 cm^{-1} (br, vs)

analysis and IR spectra. Reaction of $(COD)_2Ni$ and $LiPR_2$ in the molar ratio 1:1 with ethylene leads to formation of the lithium phosphide-nickel(0) complex in which the phosphorus atom is bound to only one $Ni^0(C_2H_4)_2$ group.

$$(COD)_2Ni + LiPR_2 + 2\ C_2H_4 \xrightarrow[-30\,°C]{THF} (3) + 2\ COD$$

(3a) $(THF)_3Li{-}P(C_6H_{11})_2Ni(C_2H_4)_2$, $\tau_{CH_2=CH_2} = 7.7$

(3b) $[Li(THF)_4]^{\oplus}\ [(C_6H_5)_2PNi(C_2H_4)_2]^{\ominus}$, $\tau_{CH_2=CH_2} = 7.7$

The specific conductivities of the complexes *(1)* and *(3)* (0.25 M in THF at −30 °C) are *ca.* $10^{-3}\ \Omega^{-1}\ cm^{-1}$ for *(1)* and *ca.* $10^{-4}\ \Omega^{-1}\ cm^{-1}$ for *(3)* in the series:

$$\sigma_{(1a)} \approx \sigma_{(1b)} \gg \sigma_{(3b)} > \sigma_{(3a)}$$

As expected the complexes *(1)* prove to be the stronger electrolytes, since both donor orbitals of the phosphorus interact with $Ni^0(C_2H_4)_2$ groups and as a consequence there is hardly any chance for interaction with the lithium cation. The greater conductivity of *(3b)* compared to that of *(3a)* can be explained in terms of a higher stabilization of the anion by the two phenyl groups bound to the phosphorus.

Whether the Li—P bond in *(3a)* can be utilized for introduction of other metal centers is at present under investigation.

Experimental:

A mixture of $(COD)_2Ni$[4] (2.75 g, 10 mmol) and $LiP(C_6H_{11})_2$[3] (1.02 g, 5 mmol) in tetrahydrofuran (20 ml) is stirred at −30°—0 °C under ethylene until a clear solution is obtained. After addition of diethyl ether *(1a)* crystallizes at −80 °C (16 h) [yield 3.25 g (90 %)]. *(1a)* and *(3a)* have limited stability at room temperature.

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CAS Registry numbers:
(1a), 60349-40-8; *(1b)*, 60372-85-2; *(2a)*, 60349-42-0; *(2b)*, 60349-44-2; *(3a)*, 60385-02-6; *(3b)*, 60349-46-4; $(COD)_2Ni$, 1295-35-8; ^{31}P, 7723-14-0

[1] *S. D. Robinson,* MTP Int. Rev. Sci. Inorg. Chem. Ser. I, Vol. 6, 121 (1972).
[2] *K. Jonas, K. R. Pörschke, C. Krüger* and *Y.-H. Tsay,* Angew. Chem. *88*, 682 (1976); Angew. Chem. Int. Ed. Engl. *15*, 621 (1976).
[3] *K. Issleib* and *A. Tzschach,* Chem. Ber. *92*, 1118 (1959).
[4] *B. Bogdanović,* M. Kröner and *G. Wilke,* Justus Liebigs Ann. Chem. *699*, 1 (1966).

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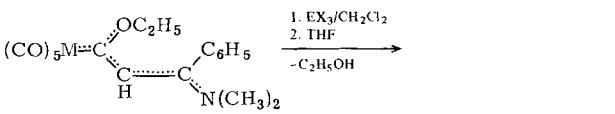
3-Dimethylamino-3-phenylallenylidene, A Novel Ligand at the Pentacarbonyl-chromium and -tungsten Skeleton[1]

By *Ernst Otto Fischer, Hans-Jürgen Kalder, Albin Frank, Frank Herwig Köhler*, and *Gottfried Huttner*[*]

Stepwise reaction of the carbene complexes pentacarbonyl(3-dimethylamino-3-phenyl-1-ethoxy-2-propenylidene)-chromium *(1)* and -tungsten *(2)*[2] with a Lewis acid (BF_3, $Al(C_2H_5)_3$) and a weak base (tetrahydrofuran) leads by 1,2 elimination of ethanol to formation of pentacarbonyl-(3-dimethylamino-3-phenylallenylidene)chromium *(3)* and -tungsten *(4)*, respectively.



(1) M = Cr, EX_3 = BF_3 *(3)*
(2) M = W, EX_3 = $Al(C_2H_5)_3$ *(4)*

The novel compounds *(3)* and *(4)* are to our knowledge the first transition-metal complexes containing "cumulogous carbene ligands"[8]. Composition and structure of these red-violet complexes are confirmed by elemental analysis, IR, NMR and mass spectra and, in the case of *(3)*, by an X-ray structure analysis[3] (Fig. 1).

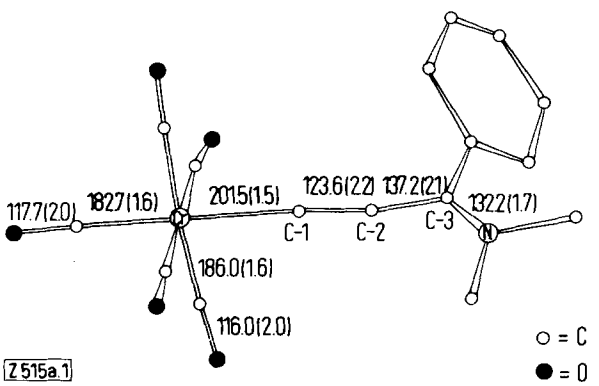
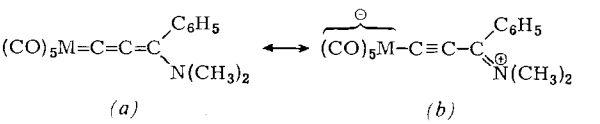


Fig. 1. Molecular structure of the allenylidene-chromium complex *(3)*.

The metal-carbon bond length in the almost linear heterocumulene moiety of *(3)* is nearly the same size as in phenyl(methoxy)carbenepentacarbonylchromium[4] corresponding to a bond order of between 1 and 2. This, and the very short (C-1)—(C-2) and (C-3)—N bond lengths indicate a considerable contribution of the mesomeric structure (b).



(a) *(b)*

The same conclusions can be drawn from the following spectroscopic results in the case of the tungsten complex *(4)*.

As in dialkylaminocarbene complexes[5] the position of the most intense ν_{CO} absorption (E) at 1923 cm^{-1} in the IR spectrum (in THF) is characteristic for a relatively high negative partial charge at the metal, the appearance of two different ^{1}H-NMR signals for the two NCH_3 groups at $\delta = 3.33$ and 3.75 ppm (in $CDCl_3$) for a partial double bond between C-3 and the dialkylamino group.

The ^{13}C resonances of the carbonyl ligands and the three allenic carbon atoms (Table 1) can be unambiguously assigned only on the basis of the ^{183}W-^{13}C coupling constants[6].

Table 1. ^{13}C-NMR spectrum of the allenylidenetungsten complex *(4)* at 305 K in $[D_8]$-THF (section).

	C-1	C-2	C-3	CO_{cis}	CO_{trans}
δ [ppm]	198.9	121.3	157.5	198.4	204.3
J (^{183}W-^{13}C) [Hz]	102.5	26.9	<5	124.5	131.8

The polarization of the cumulene system is easily recognizable from the chemical shifts; moreover, there is notable similarity in the bonding of the allenylidene and of carbonyl ligands (cf. resonance formulas (a) and (b)) as shown by δ(C-1) and $^1J(^{183}W\text{-}^{13}C\text{-}1)$. However, in accordance with the difference in bond orders the ^{183}W-^{13}C coupling constant for CO_{trans} is larger than that for CO_{cis}. Hence in agreement with the IR and ^{1}H-NMR data—there must, in contrast to the two known vinylidene ligands[7], be a higher σ-donor/π-acceptor ratio for the dimethylamino-3-phenylallenylidene ligands than for carbon monoxide. Thus (especially from the point of view of the bonding at C-3) *(3)* and *(4)* can be regarded as cumulogous carbene complexes.

Experimental:

All work must be carried out under nitrogen and with dried (Na, P_4O_{10}) as well as N_2-saturated solvents.

(3): BF_3 is injected for 10 min, into a stirred solution of *(1)* (570 mg, 1.44 mol) in CH_2Cl_2 (15 ml) at −78 °C. The mixture is concentrated to 2 ml in a high vacuum with warming to −30 °C and the adduct precipitated with 30 ml pentane and dried briefly in a high vacuum. The residue is taken up in THF, chromatographed in ether/THF on silica gel at 10 °C, and recrystallized from THF/pentane: red-violet crystals, decomposition above 125 °C; yield 150 mg (30 %).

(4): A mixture of *(2)* (1.4 g, 2.66 mmol) and $Al(C_2H_5)_3$ (0.36 ml, 2.64 mmol) in CH_2Cl_2 (30 ml) is stirred at room temperature for 5 h. The solvent is removed, the residue taken up in THF and purified in the same way as *(3)*: red-violet crystals, decomposition above 132 °C (m.p. 151 °C); yield 410 mg (32 %).

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CAS Registry numbers:
(1), 60349-49-7; *(2)*, 60349-50-0; *(3)*, 60349-51-1; *(4)*, 60349-52-2; ^{13}C, 14762-74-4

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[1] Transition Metal-Carbene Complexes, Part 95.—Part 94: *E. O. Fischer, W. Kleine*, and *F. R. Kreissl*, Angew. Chem. *88*, 646 (1976); Angew. Chem. Int. Ed. Engl. *15*, 616 (1976).
[2] *E. O. Fischer* and *H. J. Kalder*, in preparation.
[3] 1869 independent reflections ("Syntex P21"); solution with "Syntex XTL" ($R_1 = 0.067$). Cell parameters: space group P21/c; $a = 747.9$, $b = 2078.9$, $c = 1091.6$ pm; $\beta = 102.73°$; $Z = 4$; $d_{calc} = 1.40$ g cm^3; $V = 1655.47 \times 10^6$ pm^3.
[4] *O. S. Mills* and *A. D. Redhouse*, J. Chem. Soc. *A 1968*, 642.
[5] *D. J. Cardin, B. Cetinkaya*, and *M. F. Lappert*, Chem. Rev. *72*, 545 (1972).
[6] *F. H. Köhler, H. J. Kalder*, and *E. O. Fischer*, J. Organomet. Chem. *85*, C 19 (1975); *ibid. 113*, 11 (1976).
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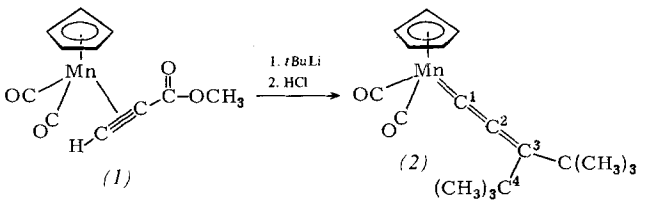
Simple Synthesis of Dicarbonyl(η-cyclopentadienyl)-(3,3-di-*tert*-butylallenylidene)manganese

By *Heinz Berke*[*]

Studies on the reaction behavior of acetylene derivatives bound to a coordinatively saturated metal center have so far not been reported in the literature. Dicarbonyl(η-cyclopentadienyl)(methylpropiolate)manganese *(1)*, which is readily accessible by photochemical synthesis at −30 to −40°C in ether, was allowed to react with *tert*-butyllithium in ether at −20 to −30°C, whereupon an acetylide complex was probably formed as intermediate; after protolysis, dicarbonyl(η-cyclopentadienyl)(3,3-di-*tert*-butylallenylidene)manganese *(2)* could be isolated in high yield as a very stable end product.



(1) *(2)*

The red-brown crystalline dialkylallenylidene complex[1] *(2)*, m. p. 121—122°C, can be purified by vacuum sublimation at 35—50°C. Its composition and structure follows from elemental analysis and spectroscopic (IR, MS, ^{1}H- and ^{13}C-NMR) findings.

In addition to the absorptions of the carbonyl ligands (1995 s(A') and 1940 cm^{-1} s(A''), soln. in *n*-hexane; 1972 s(A') and 1904 cm^{-1} s(A''), solid, KBr), the IR spectrum contains a further band in the 5 μm region which is assigned to the C=C=C group (ν_{as}(C=C=C) 1922 cm^{-1} m, soln. in *n*-hexane; 1875 cm^{-1} m, solid, KBr). The ^{1}H-NMR spectrum shows in addition to the singlet for the C_5H_5 protons (4.75 ppm; C_6D_6, TMS), only one signal for the two *tert*-butyl groups (1.33 ppm; C_6D_6, TMS) which displays no noticeable changes from −90°C to +90°C. Presumably rotation of the allenylidene ligand about the Mn—C bond is unhindered. Assignment of the seven signals in the ^{1}H broad-band decoupled ^{13}C-NMR spectrum is simplified by the fact that two signals of ^{13}C nuclei not coupled with protons are considerably broadened by coupling with ^{55}Mn (CO and C-1). Noteworthy is the extraordinarily large chemical shift for C-1, which is to be interpreted in terms of only partial compensation of the electron deficit of this atom by metal back-bonding and by conjugation to the cumulene system[1, 2].

Chemical shifts in the ^{13}C-NMR spectrum of *(2)* at 20°C in C_6D_6 rel. to TMS.

	CO	C_5H_5	C-1	C-2	C-3	C-4	CH_3
δ [ppm]	229.79	88.37	331.18	213.61	167.51	45.11	31.58

The mass spectrum of *(2)* contains the molecular ion at *m/e* = 326 and fragments due to successive loss of CO, fragmentation in the allenylidene ligand, and complete cleavage of the latter. A mass peak at *m/e* = 300 could be due to dimerized allenylidene. In fact, yellow tetra-*tert*-butylhexapentaene[3] [IR(CCl_4): 2960, 2920, 2870, 2030, 1997, 1943 cm^{-1}; ^{1}H-NMR (CCl_4, TMS): δ = 1.28 ppm] can be isolated either from the residue of the sublimation of *(2)* or directly by thermolysis of *(2)* at 100°C and normal pressure, subsequent vacuum sublimation at 80°C and crystallization from ethanol (yield 52%).

Experimental:

A solution of $C_5H_5Mn(CO)_3$ (1.5 g, 7.35 mmol) in diethyl ether (250 ml) is irradiated under protective gas in a circulation vessel at −50 to −60°C with a mercury high-pressure lamp for 2 h. To the red solution is added 1 ml (11.07 mmol) methyl propiolate and the mixture warmed to room temperature. After removal of solvent the residue is chromatographed on silica gel under protective gas. Residual $C_5H_5Mn(CO)_3$ is eluted as a first zone with petroleum ether/CH_2Cl_2 (3:1), and thereafter the orange zone of *(1)* with petroleum ether/CH_2Cl_2 (1:2); yield of almost pure *(1)*: 1.32 g (71%) [IR (*n*-hexane): 2030 w (C≡C), 1995 s, 1940 s (C≡O), 1707 cm^{-1} m (>C=O); ^{1}H-NMR (C_6D_6, TMS): δ = 3.5 (CH_3), 4.11 (C_5H_5), 5.71 ppm (CH); MS: *m/e* = 260 (M^+)].

A solution of *tert*-butyllithium (8.31 mmol) in hexane is added under protective gas at −20 to −30°C to a stirred solution of *(1)* (720 mg, 2.77 mmol) in ether (100 ml). After 0.5 h the reaction mixture is treated with ethereal hydrochloric acid and filtered from LiCl at room temperature. After removal of solvent the residue is sublimed in a vacuum, firstly at 35°C and then at 50°C, the first oily portion being discarded; yield of *(2)*, 810 mg (89.5%).

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(1), 60349-48-6; *(2)*, 60372-86-3; $C_5H_5Mn(CO)_3$, 12079-65-1; ^{13}C, 14762-74-4; *tert*-BuLi, 594-19-4

[1] Almost simultaneously, 3-dimethylamino-3-phenylallenylidene complexes were synthesized independently *via* another route: *E. O. Fischer, H. J. Kalder, A. Frank, F. H. Köhler*, and *G. Huttner*, Angew. Chem. *88*, 683 (1976); Angew. Chem. Int. Ed. Engl. *15*, 623 (1976).

[2] Cf. also *L. J. Todd* and *J. R. Wilkinson*, J. Organomet. Chem. *77*, 1 (1974).

[3] *H. D. Hartzler*, J. Am. Chem. Soc. *93*, 4527 (1971).

Monochlorides of the Lanthanoids: GdCl and TbCl

By *Arndt Simon, Hansjürgen Mattausch*, and *Norbert Holzer*[*]

So far the compound Gd_2Cl_3 has represented the most metal-rich rare-earth halide. On account of metal-metal bonding Gd_2Cl_3 contains unusual structural units[1] which should be capable of variation and thus lead to a broad chemistry of reduced rare-earth metal halides (X/M < 2)[2]. Investigations have led to isolation of the isostructural Tb_2Cl_3 and shown that both compounds can be reduced further with formation of the monohalides. GdCl and TbCl are formed on heating the respective metals with their trichlorides to 800°C in a sealed tantalum vessel. Both compounds form graphite-colored, crystalline platelets and are isotypic with ZrCl[3].

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The terbium compound has the analytically determined composition $TbCl_{1.09\pm0.04}$. The crystals decompose in moist air and react in water with evolution of hydrogen. According to the structure, GdCl and TbCl are expected to display two-dimensional metallic conductivity; to check this, however, larger crystals than could previously be obtained are required. There is already evidence for metal-rich halides of other lanthanoids too[*].

Data from single crystal and powder diffraction are listed in Table 1 for the new compounds.

Table 1. Lattice constants according to modified Guinier photographs [4] for GdCl, TbCl and Tb_2Cl_3; preliminary atomic parameters for GdCl and TbCl; standard deviations in the last place are shown in brackets.

MCl:	space group $R\bar{3}m$; *(6c)* $z(M)\approx 0.116$, $z(Cl)\approx 0.385$	
	GdCl:	$a=3.819(1)$, $c=27.482(6)$ Å
	TbCl:	$a=3.787(1)$, $c=27.461(5)$ Å
M_2Cl_3:	space group Cm	
	Gd_2Cl_3 [1b]:	$a=15.237$, $b=3.869$, $c=10.179$ Å, $\beta=117.66°$
	Tb_2Cl_3:	$a=15.184(9)$, $b=3.869(3)$, $c=10.135(6)$ Å, $\beta=118.07(5)°$

In the monohalides close-packed double layers of metal atoms alternate with double layers of non-metal atoms (XMMX...XMMX...). Consequently there is a close relationship with the layer structures of the CdI_2 type (XMX...XMX...) as well as with the structures of Ag_2F[5], Hf_2S[6] *etc.* (XMM...XMM).

A further consideration which might also lead to an understanding of the unusual Ag_2F and Hf_2S structures is provided by a comparison with the structure of the M_2Cl_3 compounds (Fig. 1) and their resemblence to the transition-metal cluster compounds: *e.g.* MoX_2 (X = Cl, Br, I) contains Mo_6X_8 clusters linked *via* halogen bridges[7]. Decreasing the number of non-metal atoms first leads to the isolated cluster as in Mo_6Se_8[8]. Increasing the metal content further calls for M—M coupling of metal octahedra; in Mo_5As_4[9] ($\triangleq Mo_{2/2}Mo_4As_{8/2}$) "condensation" *via* opposite corners of octahedra takes place with formation of chains.

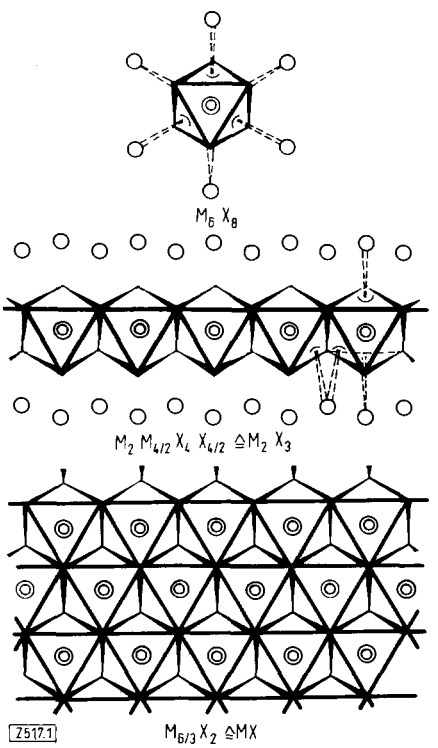

Fig. 1. Structural relationship between the rare-earth metal chlorides MX and M_2X_3 (X = Cl) and the transition-metal cluster compounds: M_6X_8 clusters are coupled *via* opposite edges in compounds M_2X_3 (octahedron chain). Further "condensation" leads to layers of octahedra in compounds MX. An XMMX layer is shown perpendicular to the projection (open circles: Cl).

Examples of cluster coupling *via* common edges are also known: thus condensation *via* neighboring edges of the M_6-octahedron leads to an arrangement like that already found in Nb_2Se[10] ($\triangleq Nb_2NbNb_{3/3}Se_{4/2}$). On the other hand, the structure of the rare-earth metal compounds M_2Cl_3 corresponds to a direct M—M coupling of oppositely situated octahedron edges ($\triangleq M_2M_{4/2}Cl_4Cl_{4/2}$). The structure of the monochloride MCl (Fig. 1) can be derived easily by further condensation. The metal-atom double layers consist of M_6 octahedra coupled edge to edge on all sides. Two oppositely situated faces of each octahedron are (as in the M_6X_8 group) occupied by halogen atoms ($\triangleq M_{6/3}Cl_2$). Interestingly, the arrangement of atoms around every individual M_6 octahedron is the same in the rare-earth metal halides as in the M_6X_8 cluster, with the exception that six of the non-metal atoms are replaced by metal atoms of a neighboring octahedron (cf. Fig. 1).

Structural considerations point to bonding analogies between lanthanoids and some 4d- and 5d-metals. The necessity of a higher metal content as a requisite for cluster formation in lanthanoids (small number of valence electrons) leads automatically to condensed cluster systems in the case of these elements.

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CAS Registry numbers:
GdCl, 40603-48-3; TbCl, 60363-74-8; Tb_2Cl_3, 60427-55-6

[1] a) *J. E. Mee* and *J. D. Corbett*, Inorg. Chem. *4*, 88 (1965); b) *D. A. Lokken* and *J. D. Corbett*, *ibid. 12*, 556 (1973).
[2] *A. Simon*, Chem. Unserer Zeit *10*, 1 (1976).
[3] *S. I. Troyanov*, Vestn. Mosk. Univ. Khim. *28*, 369 (1973); *D. G. Adolphson* and *J. D. Corbett*, Inorg. Chem., in press.
[4] *A. Simon*, J. Appl. Crystallogr. *3*, 11 (1970).
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[*] *Note added in proof:* Simultaneously *Corbett et al.* prepared ScCl and ScBr (private communication). In the meantime we have prepared and characterized ErCl ($a=3.781$, $c=28.008$ Å) and LuCl ($a=3.722$, $c=27.846$ Å).

Photochemical Liberation of 1-Naphthylamine from *cis*-Dichlorobis(1-naphthylamino)platinum(II)[**]

By *Arnd Vogler* and *Alfred Kern*[*]

While aromatic amines in the ground state are good bases, the electron density at the amine nitrogen is drastically reduced in the first excited singlet state[1]. We have now been able to show for the first time that an aromatic amine consequently loses its ability to coordinate to a metal on absorption of light and is therefore liberated from a complex.

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The complex *cis*-Pt(II)(1-naphthylamine)$_2$Cl$_2$ was synthesized by reaction of K_2PtCl_4 with 1-naphthylamine in water/dimethylformamide (DMF) and obtained analytically pure by recrystallization. The *cis* assignment (C_{2v}) follows from the presence of two IR bands (339 and 328 cm^{-1}) in the Pt—Cl stretching frequency range[2]. The photochemical behavior of the complex is also compatible only with a *cis* geometry. In the absorption spectrum the intense $\pi\pi^*$-intraligand band of the coordinated amine appears at 293 nm and the first LF band as a weak shoulder at 380 nm.

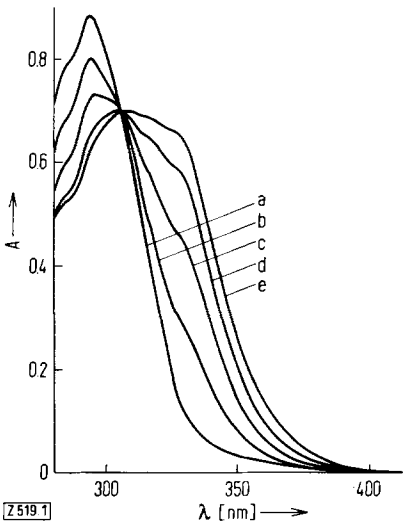

Fig. 1. Change in the absorption spectrum during the photolysis of a solution of the complex *cis*-Pt(1-naphthylamine)$_2$Cl$_2$ (7.2×10^{-5} mol/liter) in H_2O/DMF (50:50) in a 1-cm cell. Excitation source: $\lambda>280$ nm; duration of irradiation: a, 0; b, 1.5; c, 2.25; d, 3.75; e, 6 min.

Irradiation of *cis*-Pt(1-naphthylamine)$_2$Cl$_2$ dissolved in H_2O/DMF with light of wavelengths >280 nm leads to liberation of the amine which was detected by its fluorescence ($\lambda_{max}=440$ nm) and conversion into an azo dye. The change in the absorption spectrum of *cis*-Pt(1-naphthylamine)$_2$Cl$_2$ with increasing duration of irradiation displays an isosbestic point at 307 nm (Fig. 1). If substitution of naphthylamine by a solvent molecule (S) according to

cis-Pt(1-Naphthylamine)$_2$Cl$_2$ + S →
cis-Pt(1-Naphthylamine)(S)Cl$_2$ + 1-Naphthylamine

is the sole photochemical reaction, then the intraligand absorptions of the complexed naphthylamine ligands in the starting and the product complex should be additive because the naphthylamine ligands in both complexes are situated *trans* to the same ligand (chloride) and are therefore engaged in the same kind of bonding due to the *trans* effect in square-planar complexes[2]. This assumption could be substantiated by simulation of the spectral change. Mixtures of *cis*-Pt(1-naphthylamine)$_2$Cl$_2$ and free 1-naphthylamine in various ratios but with a constant total concentration gave rise to the same spectral changes as in Figure 1. This additivity would not be expected for substitution of chloride or a *cis/trans* isomerization since the change of the ligand situated *trans* to the naphthylamine would have modified the position and the intensity of the intraligand band. The substitution of chloride and the isomerization but not the release of amine are initiated by excited LF or CT states of comparable Pt(II) complexes[3].

The quantum yield was determined by initiating the reaction by excitation at two wavelengths (280 and 313 nm) lying within the absorption band of coordinated 1-naphthylamine. A value of $\phi=0.1\pm0.02$ was obtained in each case. Radiation of 435-nm light into the LF band did not lead to substitution of 1-naphthylamine ($\phi<10^{-3}$).

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CAS Registry number:
cis-Pt(1-Naphthylamine)$_2$Cl$_2$, 60525-63-5

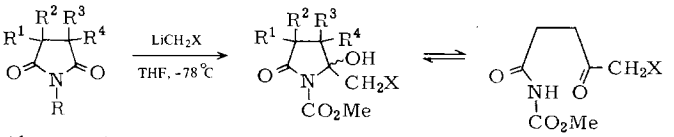
[1] *N. Mataga*, Bull. Chem. Soc. Jpn. *36*, 654 (1963).
[2] *T. G. Appleton, H. C. Clark*, and *L. E. Manzer*, Coord. Chem. Rev. *10*, 335 (1973).
[3] *P. Natarajan* and *A. W. Adamson*, J. Am. Chem. Soc. *93*, 5599 (1971); and references cited therein.

Reaction of *N*-Protected Succinimides with α-Lithiated Acetic Acid Derivatives[**]

By *Albert Gossauer*, *Wolfgang Hirsch*, and *Reinhard Kutschan*[*]

Succinimides are known to react at one—occasionally at both—carbonyl group(s) with alkyl- or alkynyl-Grignard reagents as well as under the conditions of the Reformatsky, Wittig, or Horner reactions[1]. Owing to the acidity of the hydrogen atom bonded to the nitrogen, however, only *N*-substituted derivatives react with both Grignard reagents and non-resonance-stabilized phosphorus ylides. Although *N*-unsubstituted succinimides react with the slightly basic cyanomethylenetriphenylphosphorane high temperatures (about 200 °C) are necessary to obtain reasonable yields of the desired products (cf. [1]).

We have found that succinimides *(2)* which are protected by a methoxycarbonyl group attached to the nitrogen atom readily react at −78 °C with α-lithiated acetic acid derivatives (cf. Table 1). After reaction, the protecting group can be smoothly removed by treatment of the product with $NaHCO_3$ in boiling methanol.



(1), R = H
(2), R = $COOCH_3$

(3)

(4)

(a), $R^1=R^2=R^3=R^4=H$; *(b)*, $R^1=R^3=H$, $R^2=R^4=CH_3$ (*trans*)
(c), R^1, $R^2=CH_3$-CH=(*E*), $R^3=CH_3$, $R^4=H$
X = $CO_2C_2H_5$, CO_2-*t*-Bu, CN

Table 1. Non-optimized yields of the reaction of *N*-(methoxycarbonyl)succinimides *(2)* with α-lithiated acetic acid derivatives ($LiCH_2X$).

X	Yield [%]		
	(3a)	*(3b)*	*(3c)*
$CO_2C_2H_5$	92	98 [a]	50 [a]
CO_2-*tert*-Bu	86	93 [a]	55 [a]
CN	45	41 [a]	38 [a]

[a] As a mixture of diastereomers.

Since γ-hydroxy lactams *(3)* may occur as tautomeric γ-oxo amides *(4)*[2], the structures of the products *(3a)* to *(3c)* were investigated by ^{13}C-NMR spectroscopy[3], a much

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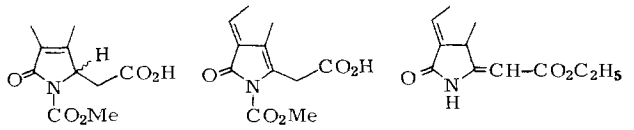
more reliable tool for the study of this kind of ring-chain tautomerism than other conventional methods[2]. Thus, compounds *(3a)*, X = $CO_2C_2H_5$ and *(3a)*, X = CO_2-*tert*-Bu[4] were found to occur in the chain form *(4)*, whereas the reaction products obtained from *(2b)* and *(2c)* are γ-hydroxy lactams *(3)*. Accordingly, cleavage of the *tert*-butyl group from *(4)*,



(5) *(6)* *(7)(Z + E)*

X = CO_2-*tert*-Bu, by means of hydrogen chloride in nitromethane at 0 °C[5] affords a β-oxo carboxylic acid derivative which readily loses carbon dioxide, whereas, under the same conditions, the γ-hydroxy lactams *(3b)* and *(3c)* yield the corresponding 5-oxopyrrolin-2-ylacetic acids *(5)* and *(6)*, respectively. The formation of *(6)* confirms the structure given for *(3c)*, X = CO_2-*tert*-Bu, which is, therefore, formed regiospecifically from *(2c)*. In contrast, thermal dehydration[6] of *(3b)* and *(3c)*, both with X = $CO_2C_2H_5$, yields the corresponding enamides [*e.g. (7)* from *(3c)*].

Experimental

Introduction of the protecting group into *(1)*: A solution of the imide *(1)*[7] in anhydrous *tert*-butanol (0.1 mol in 50 ml) is treated with a 1 M solution of potassium *tert*-butoxide in *tert*-butanol (100 ml). The solid product, obtained after removal of the solvent, is suspended in dry ether (150 ml), methyl chloroformate (30 ml) is *slowly* added dropwise to the suspension, and the mixture is heated for 5 h under reflux. The KCl which separates is filtered off, the filtrate concentrated to dryness by evaporation of the solvent, and the residue purified by crystallization, if necessary after chromatography of the crude product on silica gel with ether/*n*-hexane (7:3) as eluent.

Reaction of *(2)* with α-lithiated acetic acid derivatives ($LiCH_2X$): Lithium hexamethyldisilylamide[8] (0.1 mol) is dissolved in dry tetrahydrofuran (100 ml) and the solution is chilled to −78 °C. After ethyl acetate, *tert*-butyl acetate, or acetonitrile (0.11 mol) has been slowly dropped into the stirred solution, the mixture is stirred for further 30 min at −78 °C. To the resulting solution of the corresponding α-lithiated acetic acid derivative, is added dropwise a solution of the *N*-methoxycarbonylsuccinimide *(2)* in anhydrous tetrahydrofuran (0.05 mol in 50 ml) over 15 min. The mixture is allowed to stand for 1 h at −78 °C and then neutralized with aqueous HCl (10%) with vigorous stirring. When the solution has reached room temperature, the solvent is removed *in vacuo*, the residue disolved in CH_2Cl_2, and the remaining LiCl filtered off. After removal of the solvent, the crude product can be purified by chromatography on silica gel with ether/*n*-hexane (7:3) as eluent.

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(1a), 123-56-8; *(1b)*, 60512-08-5; *(1c)*, 28098-82-0; *(2a)*, 25543-13-9; *(2b)*, 60512-09-6; *(2c)*, 60512-10-9; *(3a)* (X = $CO_2C_2H_5$), 60512-11-0; *(3a)* (X = CO_2-*t*-Bu), 60512-12-1; *(3a)* (X = CN), 60512-13-2; *(3b)* (X = $CO_2C_2H_5$) isomer 1, 60512-14-3; *(3b)* (X = $CO_2C_2H_5$) isomer 2, 60512-15-4; *(3b)* (X = CO_2-*t*-Bu) isomer 1, 60512-16-5; *(3b)* (X = CO_2-*t*-Bu) isomer 2, 60512-17-6; *(3b)* (X = CN) isomer 1, 60512-18-7; *(3b)* (X = CN) isomer 2, 60512-19-8; *(3c)* (X = $CO_2C_2H_5$) isomer 1, 60512-20-1; *(3c)* (X = $CO_2C_2H_5$) isomer 2, 60512-21-2; *(3c)* (X = CO_2-*t*-Bu) isomer 1, 60512-22-3; *(3c)* (X = CO_2-*t*-Bu) isomer 2, 60512-23-4; *(3c)* (X = CN) isomer 1, 60512-24-5; *(3c)* (X = CN) isomer 2, 60512-25-6; *(4)* (X = $CO_2C_2H_5$), 60512-26-7; *(4)* (X = CO_2-*t*-Bu), 60512-27-8; *(5)*, 60512-28-9; *(6)*, 60512-29-0; *(Z)-(7)*, 60512-30-3; *(E)-(7)*, 60512-31-4; $LiCH_2CO_2C_2H_5$, 26954-26-7; $LiCH_2CO_2$-*t*-Bu, 41850-36-6; $LiCH_2CN$, 20428-58-4

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[2] *W. Flitsch*, Chem. Ber. *103*, 3205 (1970).
[3] The 22.63 MHz PFT ^{13}C-NMR spectra were measured in $CDCl_3$ with a HFX 90 spectrometer (Bruker-Physik AG) using the ^{19}F-resonance of C_6F_6 as internal lock signal.
[4] We thank Dr. *V. Wray* (Gesellschaft für Biotechnologische Forschung, mbH., Braunschweig) for the 25.16 MHz PFT ^{13}C-NMR spectrum of this compound.
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[6] *R. L. Shriner* in *R. Adams*: Organic Reactions. Wiley, New York 1954, Vol. 1, Chap. 1.
[7] For a synthesis of *(1c)* see *A. Gossauer* and *W. Hirsch*, Justus Liebigs Ann. Chem. *1974*, 1496.
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Synthesis of an Isomer-Free Tetravaline Derivative by Stereoselective Four-Component Condensation and Exponential Multiplication of Selectivity

By *Reinhard Urban, Gerhard Eberle, Dieter Marquarding, Dieter Rehn, Hendrik Rehn*, and *Ivar Ugi*[*]

According to the variant of the four-component condensation described in ref. [1], we have carried out the reaction of *N*-formyl-L-valine *(1)* with (*R*)-1-ferrocenyl-2-methylpropanamine *(2-R)*, 2-methylpropanal *(3)*, and *N*-(2-isocyano-3-methylbutanoyl)-L-valine methyl ester *(4)*. The diastereomeric products *(5n)* and *(5p)* were formed in the ratio 91.2:8.8. The stereoselectivity can be enhanced by addition of two mol. equiv. of tetraethylammonium *N*-formyl-L-valinate (see procedure): the ratio then increases to *(5n)*:*(5p)* = 98.5:1.5.

(5n) and *(5p)* can be resolved by chromatography on silica gel with dichloromethane/ethyl acetate (20:1) or by recrystallization from light petroleum/chloroform (10:1). A particularly effective preparation of pure *(5n)* can be accomplished by selective acidolysis of the mixture of *(5n)* and *(5p)*, which amounts to an exponential multiplication of the selectivity of the four-component condensation: *(5p)* is cleaved some 230 times faster to give *(6p)* than *(5n)* to give *(6n)* on treatment with trifluoroacetic acid and thioglycolic acid[2] (see Table 1).

Table 1. Selective acidolysis of *(5n)* + *(5p)* = 98.5:1.5 with trifluoroacetic acid in dichloromethane at 20 °C.

Duration [min]	Loss of *(5n)* [%]	Ratio *(5n)*:*(5p)* after acidolysis
2	0.1	98.8 : 1.2 [a]
10	0.5	99.5 : 0.5 [a]
28	1.2	99.93 : 0.07 [b]
85	4.2	> 99.98 : 0.02 [c]

[a] Determined gravimetrically.
[b] Determined by high pressure liquid chromatography.
[c] *(5p)* could no longer be detected in the product by thin layer chromatography, high pressure liquid chromatography, and comparison of the specific rotatory powers [detection limits of all methods *ca.* 0.02% of *(5p)* in a mixture with *(5n)*].

The time dependence of the concentrations $c_{n,t}$ and $c_{p,t}$ of *(5n)* and *(5p)* respectively is described by the equations

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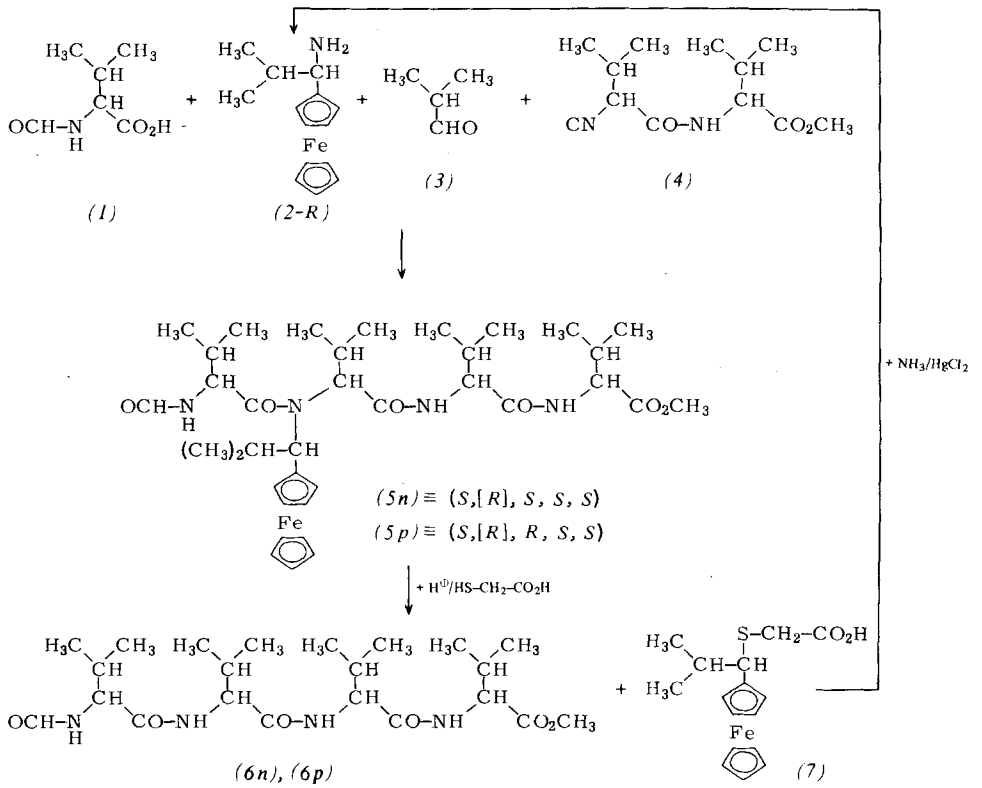

(a) and (b) [$c_{n,0}$ and $c_{p,0}$ = initial concentrations, k_n and k_p = rate constants of acidolysis].

$$c_{n,t} = c_{n,0} \cdot e^{-k_n \cdot t} \quad \text{(a)}$$

$$c_{p,t} = c_{p,0} \cdot e^{-k_p \cdot t} \quad \text{(b)}$$

With $k_p/k_t = x = 230$ and $\tau = t/t_{1/2,n}$ [where $t_{1/2,n}$ = half-life of *(5n)* = 1500 min] we obtain eq. (c).

$$c_{n,\tau}/c_{p,\tau} = (c_{n,0}/c_{p,0}) \cdot 2^{(x-1)\cdot\tau} \quad \text{(c)}$$

The selectivity multiplication factor

$$V = 2^{(x-1)\tau}$$

increases steeply and indefinitely for $x > 1$ and $\tau \geq 0$ with increasing duration of reaction and it becomes possible to isolate the isomer *(5n)* in extremely high purity after removal of *(6p)* and *(7)* by stopping the acidolysis at the right time. The procedure resembles the production of optically active compounds from racemates by reactions which consume one enantiomer faster than the other.

(6n) is obtained from isolated *(5n)* by renewed acidolysis in the presence of thioglycolic acid. The asymmetrically inducing amine component *(2-R)* is resynthesized from *(7)*.

Procedure:

Synthesis of *(5n)* and *(5p)*: *(2-R)* (2.57 g, 10 mmol) is dissolved in anhydrous ether (20 ml) and freshly distilled *(3)* (0.8 g, 11 mmol) then added at 20 °C. Water produced is removed with a molecular sieve (4 Å). After 2 h the reaction mixture is evaporated *in vacuo* and the residue dissolved in anhydrous methanol (500 ml). To the stirred solution at −78 °C are successively added dropwise the isocyanide component *(4)* (2.4 g, 10 mmol) dissolved in anhydrous methanol (200 ml) and *(1)* (1.45 g, 10 mmol) and tetraethylammonium *N*-formyl-L-valinate (5.5 g, 20 mmol) together dissolved in anhydrous methanol (300 ml). After reacting for 35 h at −78 °C the mixture is poured into water (500 ml), extracted with ether, the ether phase washed with a 3 % aqueous solution of tartaric acid, 0.5 N aqueous NaOH, and water, and concentrated *in vacuo*. Yield of *(5n)* + *(5p)* = 43 %. Resolution of *(5n)* and *(5p)* was accomplished by chromatography over kieselgel 60 (Merck: 70 to 230 mesh) with dichloromethane/ethyl acetate (20:1).—*(5n)*: m.p. 163 to 164 °C, $[\alpha]_D^{20} = +152.1°$, $[\alpha]_{546}^{20} = +298.7°$ ($c = 1.3$, C_2H_5OH).—*(5p)*: m.p. 165 °C, $[\alpha]_D^{20} = +412.7°$, $[\alpha]_{546}^{20} = +671.8°$ ($c = 1.7$, C_2H_5OH).

Selective acidolysis of *(5p)*: The mixture of *(5n)* and *(5p)* (0.5 g) is dissolved in dichloromethane (20 ml), treated with trifluoroacetic acid (0.8 ml) at 20 °C, and immediately thereafter with thioglycolic acid (5 g). The reaction mixture is allowed to stand at 20 °C. Acidolysis is terminated by addition of saturated aqueous $NaHCO_3$ solution, extraction with ether, repeated extraction with water, and evaporation *in vacuo*. The residue consists of unreacted *(5n)* or, after short reaction times, a mixture of *(5n)* and *(5p)* enriched in *(5n)*.

Acidolysis of *(5n)*: The same procedure is adopted as for the mixture of *(5n)* and *(5p)* and the reaction is allowed to progress until *(5n)* can no longer be detected by thin layer chromatography. The solution is extracted with water, the extract neutralized and shaken with dichloromethane. Vacuum evaporation of the dichloromethane extract affords *(6n)* in 92 % yield based on *(5n)*. M.p. 176 °C, $[\alpha]_D^{20} = -47.2°$, $[\alpha]_{546}^{20} = -52.0$ °C ($c = 0.2$, C_2H_5OH).

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[1] *R. Urban* and *I. Ugi*, Angew. Chem. 87, 67 (1975); Angew. Chem. Int. Ed. Engl. 14, 61 (1975).
[2] *G. Eberle* and *I. Ugi*, Angew. Chem., in press.

Synthesis of 1,2,3,5-Hexatetraene[1]

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Linear C_6H_6 hydrocarbons are preparatively useful starting materials in hydrocarbon chemistry and are suitable model

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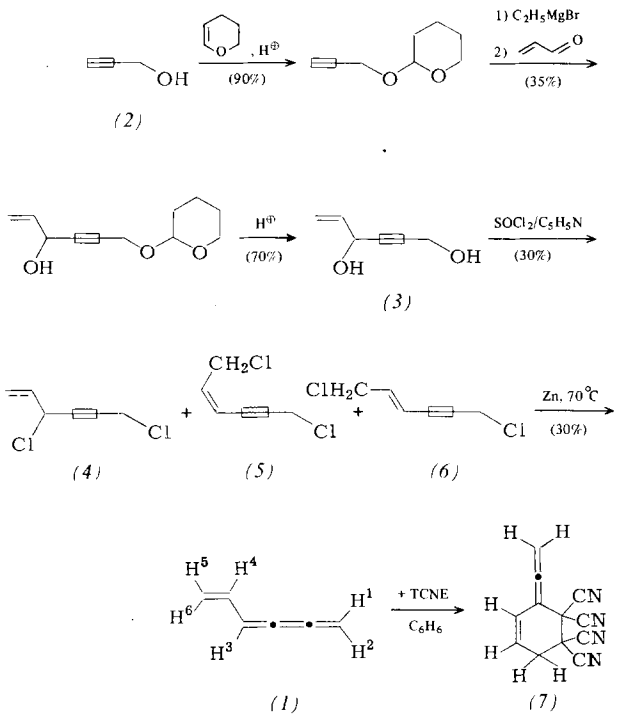
substances for spectroscopic investigations. A total of twelve such linear "acyclic benzene isomers" may be formulated, ten of which are already known[2]. We report here on the synthesis of 1,2,3,5-hexatetraene *(1)*, the penultimate member of this series of compounds[3]. The tetraene *(1)* is a monosubstituted[3] cumulene and thus belongs to a group of highly reactive polyolefins, about which little is known.

In analogy to a procedure described by *Arens et al.*[4], *(1)* was synthesized as follows: propargyl alcohol *(2)* was converted, *via* the intermediates shown in the scheme, into the diol *(3)*[5]. Reaction of *(3)* with thionyl chloride/pyridine afforded the isomeric dichlorides *(4)* to *(6)*, which were separated gas chromatographically on an Apiezon column (140 °C) and identified by the usual spectroscopic methods[5] (product ratio *(4)*: [*(5)*+*(6)*] = 60:40).



Dechlorination and rearrangement of the unseparated dichloride mixture was accomplished by treatment with zinc dust in diethylene glycol dibutyl ether[6] at 70 °C. The compound *(1)* was quickly removed from the reaction flask (at *ca.* 0.1 torr) as it formed, and allowed to freeze out in a nitrogen-cooled trap (yield of crude product 30 %). Fractional re-condensation in a high-vacuum unit afforded pure *(1)* as a colorless liquid stable at −78 °C in the absence of oxygen. When the temperature is allowed to exceed −40 °C exothermic decomposition rapidly sets in, accompanied by a change in color of the liquid product from colorless through brilliant yellow and brown to black. Dilute solutions of *(1)* in dichloromethane or ether, on the other hand, are stable for several hours at −10 °C. In the NMR spectrum (−40 °C, $CDCl_3$) of *(1)*, which according to the mass spectrum has a molecular weight of 78, there appear two complex multiplets, one between $\delta = 6.56$ and 6.08 (2H) the other between 5.62 and 5.00 (4H); these can be ascribed to the protons H^3 and H^4 and H^1, H^2, H^5, and H^6, respectively. The vibrational spectrum (in $CDCl_3$), which contains very few bands, shows maxima at 2040 and 825 cm^{-1} (—CH=C=C=CH_2) as well as at 3080, 3000, 1605, 1005, and 980 cm^{-1} (—CH=CH_2). Attempts to carry out an elemental analysis and to record a quantitative electron spectrum failed due to the instability of *(1)*. Nevertheless, the band positions and shape of the qualitative spectrum (in ethanol) [$\lambda_{max} = 228$ (weak) and 278 nm (strong)] are in accord with the UV spectra of the other [3]cumulenes[7].

For chemical structure proof, *(1)* was trapped with tetracyanoethylene in dichloromethane at −78 °C. The Diels-Alder adduct *(7)* (white platelets from ethanol, m.p. 130—131 °C) was formed, whose structure was confirmed spectroscopically[5] as well as by elemental analysis.

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(1), 60239-33-0; *(2)*, 107-19-7; *(3)*, 60239-34-1; *(4)*, 60239-35-2; *(5)*, 60239-36-3; *(6)*, 60239-37-4; *(7)*, 60239-38-5; tetracyanoethylene, 670-54-2

[1] Part 6 of Alkynes and Cumulenes. This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft and carried out at the Institut für Organische Chemie der Universität Karlsruhe.—Part 5: *U. Mödlhammer* and *H. Hopf*, Angew. Chem. *87*, 492 (1975); Angew. Chem. Int. Ed. Engl. *14*, 501 (1975).

[2] *H. Hopf*, Chem. Ber. *104*, 1499, 3087 (1971); *H. Maurer*, Diplomarbeit, Universität Karlsruhe 1973, and Dissertation to be presented in 1976 at the Universität Karlsruhe.

[3] The isomer to be prepared is 1,2,3,4-hexatetraene.

[4] *J. F. Arens, L. Brandsma*, and *P. P. Montijn*, Rec. Trav. Chim. Pays-Bas *86*, 127 (1967).

[5] Correct elemental analyses were obtained for the new substances.

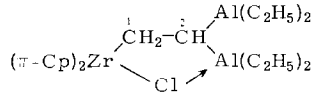
[6] *E. Kloster-Jensen* and *J. Wirz*, Helv. Chim. Acta *58*, 162 (1975).

[7] *F. Bohlmann* and *K. Kieslich*, Chem. Ber. *87*, 1363 (1954); *W. J. Ball, S. R. Landor*, and *N. Punja*, J. Chem. Soc. *C 1967*, 194.

Extreme Bond Angle Distortion in Organozirconium Compounds Active Toward Ethylene[**]

By *Walter Kaminsky, Jürgen Kopf, Hansjörg Sinn*, and *Hans-Jürgen Vollmer*[*]

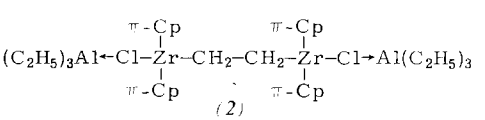
We have recently reported on the structure of *Al,Zr*-μ-chloro-1-[dicyclopentadienylzirconio(IV)]-2,2-bis(diethylalumino)ethane *(1)*[1].



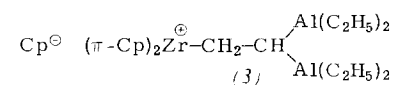
(1), Cp = Cyclopentadienyl

The angle to C-1 of the alkyl ligand substituted twice by diethylalumino groups at C-2 is only 76°; nevertheless, this can be explained by formation of a five-membered ring as a result of dative bonding between the chlorine atom and an aluminum atom. Dynamic NMR measurements showed, however, that the dative bond is not very strong[2].

We have now carried out X-ray spectrographic investigations on compound *(2)* and the compound *(3)* formed from *(1)* by replacement of chlorine by a cyclopentadienyl moiety.



(2)



(3)

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[**] Based on a lecture delivered at the Makromoleculares Kolloquium in Freiburg, March 1976.

Ring formation as in *(1)* should be impossible in these compounds.

Remarkably, it was found that the σ-bonded atomic grouping Zr—CH_2—C is always characterized by an angle of only 76° at the CH_2 group. Fig. 1 shows the corresponding atomic groupings of compounds *(1)* to *(3)* for comparison.

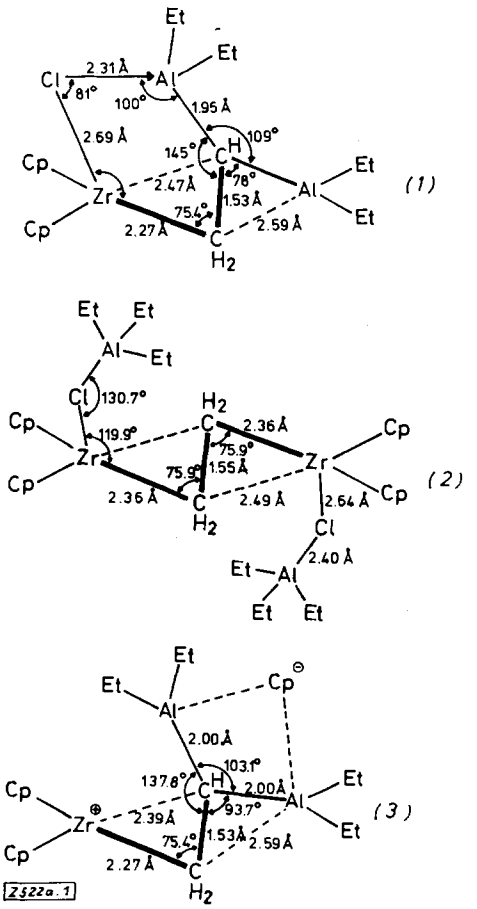

Fig. 1. Comparison of corresponding structural elements of compounds *(1)*, *(2)*, and *(3)*. Note the angle at C(1) in *(1)* and *(3)* and at C(1) and C(2) in *(2)*.

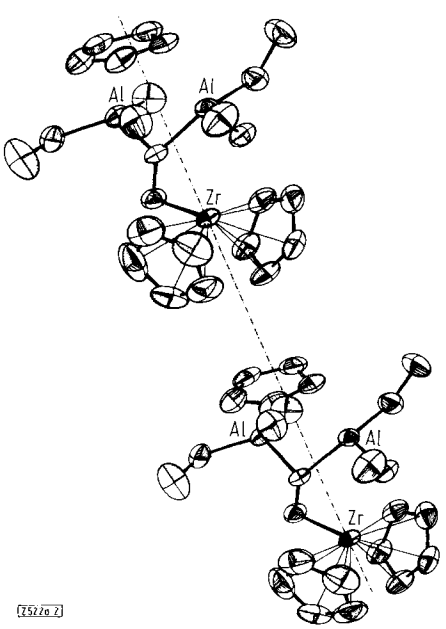

Fig. 2. ORTEP projection of two molecules of *(3)*. The *R* value is 0.03. A detailed account by *J. Kopf* is in preparation. Note the symmetrical position of the third cyclopentadienyl ring with respect to the Zr—Zr axis.

The third cyclopentadienyl ring in *(3)* shows a remarkable arrangement, completely deviating from the σ- or π-bonding cyclopentadienyl rings in bis(η-cyclopentadienyl)bis(σ-cyclopentadienyl)titanium(IV)[3] and (σ-cyclopenta-2,4-dien-1-yl)tris(η-cyclopentadienyl)zirconium(IV)[4]. It is released from $Zr(IV)^{\oplus}$ as the anion and arranged symmetrically in the lattice between two neighboring zirconium centers (Fig. 2). The ^{1}H-NMR spectrum shows singlets for the cyclopentadienyl rings of *(3)* at $\delta = 6.62$, 5.33, and 5.27 ppm in the ratio 1:1:1. The compound has a dipole moment of 5.4 Debye.

The completely halogen-free compound *(3)* is soluble in hydrocarbons and inserts α-olefins and 1,3-dienes to give compounds whose structures have so far not been elucidated.

The halogen-containing compounds *(1)* and *(2)* react with α-olefins and 1,3-dienes on addition of excess trimethylaluminum, and especially on addition of triethylaluminum and water; dehalogenation takes place, presumably with formation of alumoxanes[5], to give very active homogeneous catalysts for the polymerization of α-olefins, particularly of ethylene.

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CAS Registry numbers:
(1), 55466-98-3; *(2)*, 56379-20-5; *(3)*, 60260-47-1

[1] *W. Kaminsky, J. Kopf*, and *G. Thirase*, Justus Liebigs Ann. Chem. *1974*, 1531.
[2] *W. Kaminsky* and *H.-J. Vollmer*, Justus Liebigs Ann. Chem. *1975*, 438.
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[5] *G. B. Sakharovskaja, N. N. Korneyev, A. F. Popov, K. J. Larikov*, and *A. T. Zhigachi*, Zh. Obshch. Khim. *34*, 3478 (1964).

Halogen-Free Soluble Ziegler Catalysts for the Polymerization of Ethylene. Control of Molecular Weight by Choice of Temperature[**]

By *Arne Andresen, Hans-Günther Cordes, Jens Herwig, Walter Kaminsky, Alexander Merck, Renke Mottweiler, Joachim Pein, Hansjörg Sinn*, and *Hans-Jürgen Vollmer*[*]

Catalyst systems based on bis(cyclopentadienyl)titanium(IV) chloride with alkylaluminum chlorides or trialkylaluminum polymerize ethylene. With decreasing chlorine content their activity generally decreases while their rate of reduction increases[1]. Analogous Zr compounds, which are not reduced at room temperature, show no polymerization activity[2].

D. S. Breslow has recently shown that the activity of the known homogeneous chlorine-containing systems based on bis(cyclopentadienyl)titanium(IV) is increased on addition of water[3]. In systems completely free of chlorine, complex formation between titanium or zirconium compound and trialkylaluminum is not observed, either NMR- or UV-spectroscopically[4], or even cryoscopically[5], while in the presence of one chlorine atom per atom of transition metal [starting

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[**] Based on a lecture delivered at the Molekulares Kolloquium in Freiburg, March 1976.—The observations related in this communication have led to patent applications being made. Future license fees were covenanted to the Hansische Universitätsstiftung on the occasion of the 70th birthday of *Franz Patat*. We thank the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft for financial support of our work.

from bis(cyclopentadienyl)methyltitanium(IV) monochloride] complex formation is almost quantitative[6]. Surprisingly, however, not only halogen-deficient but also halogen-free systems exhibited β-hydrogen transfer (and α-hydrogen transfer, but much more slowly) with formation of dimetalloalkanes[7]. NMR-spectroscopic investigation of such a reaction in the presence of ethylene revealed a weak but lasting insertion of ethylene with formation of polyethylene[4b]. Addition of traces of chloride in the form of bis(cyclopentadienyl)titanium(IV) chloride lowered the yield of polyethylene, initiated the known reduction reaction to the expected extent and accelerated it[8]. On the other hand, the yield increased to 600000 g polyethylene/g titanium and the activity to 400000 g polyethylene/g titanium/h when one equivalent of trimethyl- or triethylaluminum previously treated with water was added to dialkylbis(cyclopentadienyl)titanium(IV) [alkyl, *e.g.* methyl] (cf. Table 1 and example 1).

sence of ethylene leads to slow degradation of the starting compound (curve A_3).

If, on the other hand, addition is carried out in the presence of ethylene a long-wave absorbing species with a band maximum at 390 nm (curves A_4 and A_5) is formed in the course of a few minutes. The rate of formation of the compound characterized by $\lambda_{max} = 390$ nm is strongly dependent on the concentration of the reaction partners.

If trimethylaluminum previously treated with water is added in the presence of propylene (Fig. 1b) degradation of the starting compound is observed. Polypropylene was not found. On removal and replacement of the propylene by ethylene the maximum arises at 390 nm and polymerization of the ethylene ensues. That is, the band at 390 nm is formed only on simultaneous presence of halogen-free bis(cyclopentadienyl)titanium(IV) with water-treated trialkylaluminum and ethylene (Fig. 1c).

Table 1. Ethylene polymerization with the system bis(cyclopentadienyl)dimethyltitanium(IV), trimethylaluminum, and water.

Yield of polyethylene [g/l]	Time [h]	Temp. [°C]	Titanium concentration [mol/l]	Amount of water added [mol/l]	Rel. Mol. Wt. (viscometric)
33.6	112	21	7×10^{-4}	$< 0.25 \times 10^{-3}$	3800000
43.2	1.5	21	7×10^{-4}	4.6×10^{-3}	200000
57.6	1.5	50	3.5×10^{-4}	4.6×10^{-3}	90000
34.2	1.5	12	1.1×10^{-6}	7.5×10^{-3}	—

Interestingly, compounds formed on the basis of bis(cyclopentadienyl)zirconium(IV) and exhibiting no polymerization activity—even in the case of completely dehalogenated secondary products[9]—can also become very active polymerization catalysts by addition of trialkylaluminum previously treated with water. These systems excel in that products with relative masses between a few million and a few hundred can be generated at almost constant activity by suitably choosing the reaction temperature (Table 2).

Table 2. Control of molecular weight by choice of temperature in the polymerization of ethylene with tri(cyclopentadienyl)zirconium—aluminum compounds.

Yield of polyethylene [g/l]	Time [h]	Temp. [°C]	Zirconium concentration [mol/l]	Rel. Mol. Wt. (viscometric)
81	64	50	2.2×10^{-3}	1500000
45	48	60	2.2×10^{-3}	363000
45	64	70	2.2×10^{-3}	225000
90	88	80	2.2×10^{-3}	40000
80	64	90	2.2×10^{-3}	oils and waxes [a]

[a] Predominantly α-olefins of empirical formula $C_{2n}H_{4n}$ ($n = 2, 3, 4 \ldots$).

Preliminary experiments show a maximum activity at an $Al:H_2O$ ratio of 2:1 to 5:1. Evidently water and trialkylaluminum react with each other, for the activity disappears if the $Al:H_2O$ ratio drops below 1:3, *i.e.* all alkyl groups are hydrolyzed. Presumably alumoxanes are formed[10].

Aging processes were not observed, and in particular no reduction which would be comparable to that observed under the conditions in halogen-containing systems.

If the solution of catalyst is mixed with polyethylene and the solvent removed, "gas-phase polymerization" takes place after admission of ethylene (see example 2).

We found that the spectrum of bis(cyclopentadienyl)dimethyltitanium(IV) (Fig. 1a, curve A_1) remains unaltered—aside from dilution effects (curve A_2)—on addition of trimethylaluminum (which shows no absorption) in the absence of ethylene. Addition of trimethylaluminum treated with water in the ab-

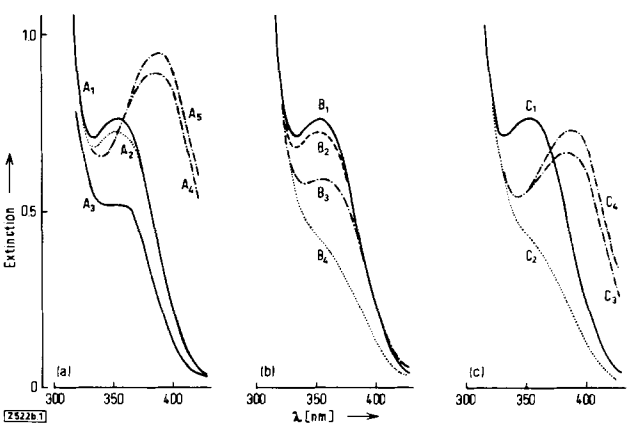

Fig. 1. UV spectroscopic measurements (Cary 14).

a) Curve A_1: 1.5 mmol $Cp_2Ti(CH_3)_2$/liter toluene. Curve A_2: A_1 + 14.4 mmol $Al(CH_3)_3$/liter toluene. Curve A_3: $A_1 + Al(CH_3)_3$ treated with H_2O (14.4 mmol/liter). Recorded after 25 min. Curve A_4: A_3 in the presence of ethylene. Recorded after 5 min. Curve A_5: A_4, recorded after 25 min.

b) Curve B_1: 1.5 mmol $Cp_2Ti(CH_3)_2$/liter toluene (=curve A_1). Curve B_2: B_1 + saturation with propylene. Curve B_3: $B_2 + Al(CH_3)_3$ treated with H_2O (14.4 mmol/liter). Curve B_4: B_3 after 5 mins.

c) Curve C_1: 1.5 mmol $Cp_2Ti(CH_3)_2$/liter toluene (=curve A_1). Curve C_2: $C_1 + Al(CH_3)_3$ treated with H_2O (14.4 mmol/liter) + saturation with propylene. Recorded after 5 min (=curve B_4). Curve C_3: C_2, propylene removed and ethylene admitted under pressure. Recorded after 7 min. Curve C_4: C_3, recorded after 16 min.

Experimental

Example 1: Trimethylaluminum (4×10^{-3} mol) and water (2.3×10^{-3} mol) are added at 12°C to 350 ml toluene in a glandless 1l agitator autoclave after careful evacuation and bake out. Bis(cyclopentadienyl)dimethyltitanium(IV) (3.7×10^{-7} mol) is then introduced and the mixture allowed to react with ethylene at 8 bar. The reaction is terminated after 90 min, and the polyethylene filtered off and dried. Yield: 11.4g. Activity: 1.11×10^6 mol ethylene per mol titanium compound

per 1.5 h. (= 644000 g polyethylene/g titanium/1.5 h = 430000 g polyethylene/g titanium/h).

Example 2: A solution of bis(cyclopentadienyl)dimethyltitanium(IV) (2.5×10^{-5} mol) in toluene (1 ml) and a solution of trimethylaluminum (5.2×10^{-3} mol) in toluene (5 ml) and water (2.6×10^{-3} mol) are added at 21 °C wall temperature to 2 g polyethylene (MW = 200000) in a glandless 1 l agitator autoclave after careful evacuation and bake out. After removal of solvent, ethylene is introduced at 8 bar. The ethylene pressure which drops to 4 bar during polymerization is increased from time to time to 8 bar. The rate of uptake of ethylene drops within the first hour to a value (about one-half the initial value) obviously determined by diffusion, and then remains constant. Since further stirring is not possible the reaction is terminated after 48 h. 49 g of polyethylene is formed. A relative molecular mass of about 4×10^6 was determined viscometrically.

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German version: Angew. Chem. 88, 689 (1976)

CAS Registry numbers:
$Cp_2Ti(CH_3)_2$, 1271-66-5; $Al(CH_3)_3$, 75-24-1; polyethylene, 9002-88-4; ethylene, 74-85-1

[1] *D. S. Breslow* and *N. R. Newburg*, J. Am. Chem. Soc. *81*, 81 (1959); *W. P. Long*, *ibid. 81*, 5312 (1959); *F. Patat* and *H. Sinn*, Angew. Chem. *70*, 496 (1958); *G. Henrici-Olivé* and *S. Olivé*, Angew. Chem. *83*, 121 (1971); Angew. Chem. Int. Ed. Engl. *10*, 105 (1971); *K. Meyer* and *K. H. Reichert*, Angew. Makromol. Chem. *12*, 175 (1970).
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[4] a) *H. Sinn*, Habilitationsschrift, Technische Hochschule München 1962; b) *R. Mottweiler*, Dissertation, Universität Hamburg 1975; c) *J. Zeysing*, Dissertation, Universität Hamburg 1975.
[5] *W. Kaminsky* and *H. Sinn*, Justus Liebigs Ann. Chem. *1975*, 424.
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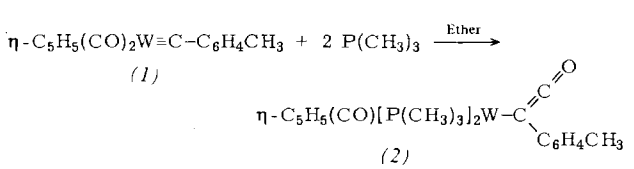
[10] *G. B. Sakharovskaja*, *N. N. Korneyev*, *A. F. Popov*, *K. J. Larikov*, and *A. T. Zhigachi*, Zh. Obshch. Khim. *34*, 3478 (1964).

Carbonyl-η-cyclopentadienyl-(4-methylphenylketenyl)-bis(trimethylphosphane)tungsten— A Novel, Stable Transition Metal-Substituted Ketene

By *Fritz R. Kreissl*, *Albin Frank*, *Ulrich Schubert*, *Tassilo L. Lindner*, and *Gottfried Huttner*[*][**]

On allowing dicarbonyl-η-cyclopentadienyl-(4-methylphenylcarbyne)tungsten *(1)*[1] to react with trimethylphosphane at −40 °C we obtained the novel transition metal substituted ketene *(2)*.



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[**] The authors wish to thank Prof. *E. O. Fischer* and the Deutsche Forschungsgemeinschaft for support of this work.

The metal-catalyzed formation of ketene moieties was previously observed in the synthesis of ketenide complexes of the type M_2C_2O (M = Cu, Ag, Au)[2]. Reactions of ketenes with carbonyl-transition metal complexes, on the other hand, led either *via* deoxygenation and/or decarbonylation to mainly polynuclear metal compounds[3] or to dicarbonyl-η-cyclopentadienyl-η-diphenylketenemanganese complexes[4].

Compound *(2)*, which precipitates as orange-yellow diamagnetic crystals, is soluble in dichloromethane but not in *n*-pentane. In solution at room temperature one of the phosphane ligands is rapidly cleaved. Composition and structure of the new ketene *(2)*[5] have been confirmed by elemental analysis, IR and NMR spectra, and by an X-ray structure analysis[6] (Fig. 1).

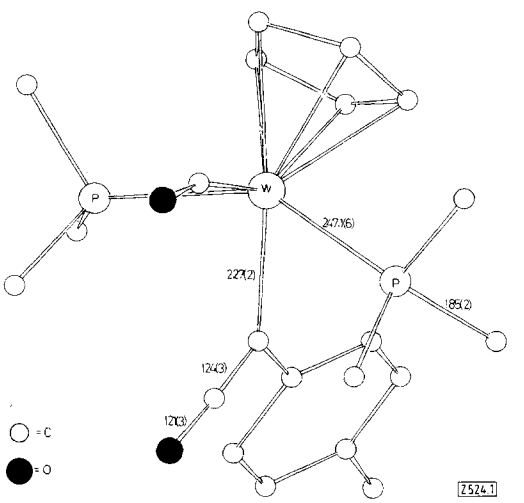

Fig. 1. Structure of ketene *(2)*.

The $W—C_{ketene}$ bond having a length of 227(2) pm is to be regarded as a single bond (for comparison: $W—C_{phenyl}$ in $\eta\text{-}C_5H_5(CO)_3W—C_6H_5$: 232 pm[7]). The lengths of the C=C- and C=O-double bonds in the ketene do not deviate significantly from those given in the literature for the free ketene [131(1) and 116(1) pm[8], respectively]. The tungsten-phosphorus distance with a value of 247.1(6) pm is shorter than the sum of the single-bond radii (W *ca.* 159 pm[9], P 110 pm[10]). The other bond lengths and angles in *(2)* correspond to the usual values.

Experimental:

All operations are carried out under nitrogen and in anhydrous (Na, P_4O_{10}) solvents saturated with N_2. A solution of *(1)* (1.02 g, 2.5 mmol) in ether (30 ml) is treated with 0.5 g (6.6 mmol) trimethylphosphane[11] at −40 °C and the mixture stirred for 36 hours. Orange-yellow crystals precipitate from the originally yellow solution. The solvent is decanted and the precipitate recrystallized from dichloromethane/pentane, washed three times with 25 ml cooled pentane, and finally dried for 10 hours at −30 °C *in vacuo*. Orange-yellow crystals, yield 86 % based on *(1)*.

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German version: Angew. Chem. 88, 649 (1976)

CAS Registry numbers:
(1), 60260-15-3; *(2)*, 60270-32-8

[1] *E. O. Fischer*, *T. L. Lindner*, and *F. R. Kreissl*, J. Organomet. Chem. *112*, C27 (1976).
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[5] Analogous phenyl- and 4-methoxyphenylketenes have also been synthesized and characterized.
[6] 1609 structure factors ($I > 3.1\sigma, \mu = 57\,cm^{-1}$; Syntex P21/XTL) $R_1 = 0.05$; monoclinic, space group $P2_1/c$, $Z = 4$, $\rho_{calc} = 1.69\,g \cdot cm^{-3}$; $a = 1272.5$, $b = 1477.5$, $c = 1522.4$ pm, $\beta = 129.6°$, $V = 2207 \times 10^6$ pm^3.
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Dimeric Bistetrathiotungstatostannate—A Novel Coordination Compound with Non-Equivalent and Tridentate WS_4^{2-} Ligands

By *Achim Müller*, *Irene Paulat-Böschen*, *Bernt Krebs*, and *Horst Dornfeld*[*]

Polynuclear complexes having metal-sulfur-metal bonds frequently present interesting aspects of structural chemistry[1]. We have now succeeded in preparing the orange colored compound *(1)* by combining solutions of $SnCl_2 \cdot 2H_2O$ and $[(C_6H_5)_4P]_2WS_4$ in dimethylformamide, and in characterizing it by elemental analysis, X-ray structure analysis, and by measurement of the vibrational spectrum. *(1)* exhibits structural features which were previously unknown.

$$[(C_6H_5)_4P)]_4[Sn_2(WS_4)_4]$$
(1)

(1) crystallizes in the triclinic space group $P\bar{1}$ with lattice parameters: $a = 14.642(3)$ Å; $b = 14.240(3)$ Å; $c = 12.895(9)$ Å; $\alpha = 94.79(4)°$; $\beta = 99.28(4)°$; $\gamma = 106.08(2)°$; $V = 2526.3$ Å^3; $Z = 1$ $[(C_6H_5)_4P]_2[Sn(WS_4)_2]$. For determining the structure the intensities of 6470 non-equivalent reflections were measured (data collection up to $\sin\theta/\lambda = 0.528$ Å^{-1}) with a Syntex-$P2_1$ four-circle diffractometer. The structure was determined by Patterson and Fourier methods and refined to an R value of 6.8% (W, Sn, S and P atoms with anisotropic temperature factors; C atoms with isotropic temperature factors).

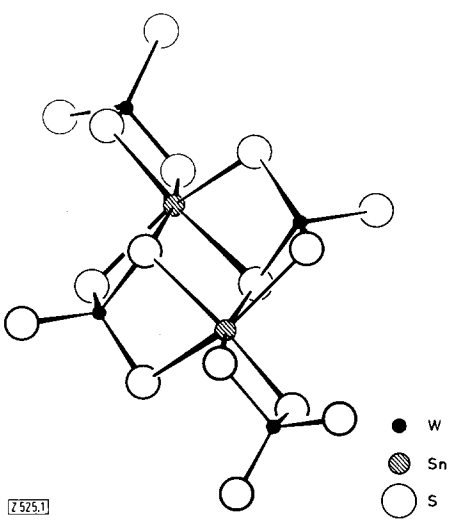

Fig. 1. Structure of the dimeric anion $[Sn_2(WS_4)_4]^{4-}$.

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Figure 1 shows the structure of the $[Sn_2(WS_4)_4]^{4-}$ complex. The anion formally contains two central SnS_6 octahedra coupled *via* a common edge. These octahedra are bonded to the four non-equivalent WS_4 tetrahedra *via* common edges. Particularly worth noting is the type of coordination of the ligands. Two of the WS_4^{2-} ions are coordinated as bidentate ligands to the Sn and possess two free S atoms. The other WS_4^{2-} ions coordinate as tridentate ligands and have only one free S atom. These tridentate WS_4 ligands contain a triply bonded sulfur atom. The SnS_6 octahedra are highly distorted, mainly due to the stereochemical influence of the lone pair on the Sn^{II}.

The bonds from W have the following lengths: to the free S atoms, 2.148(7)—2.168(7) Å; to the doubly bonded bridging S atoms, 2.178(6)—2.239(6) Å; to the triply bonded S atom, 2.212(6) Å. The distances from the Sn to the doubly bonded S atoms, 2.710(8)—3.047(8) Å, are shorter than those to the triply bonded S atoms 2.956(6) and 3.093(6) Å. The W...Sn and Sn...Sn distances are 3.508(6) and 4.647(2) Å, respectively. The four-membered WS_2Sn and SnS_2Sn ring systems are planar.

Owing to the non-equivalent WS_4^{2-} ligands, the vibrational spectrum is complex and therefore could not be used for the structure determination. The IR spectrum shows strong and characteristic bands in the WS stretching vibrations region at 491 and 485 [$\nu(WS_{free})$] as well as at 462, 440, 434, and 422 cm^{-1} [$\nu(WS_{bridge})$].

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German version: Angew. Chem. *88*, 691 (1976)
CAS Registry numbers:
(1), 60364-01-4

[1] *H. Vahrenkamp*, Angew. Chem. *87*, 363 (1975); Angew. Chem. Int. Ed. Engl. *14*, 322 (1975).

Polarogram and Reactions of a Short-Lived Oxidation Product of the Carbonate Ion

By *Michael Grätzel*, *Arnim Henglein*, *Rainer Scheerer*, and *Peter Toffel*[*]

Polarographic waves of free radicals can be observed in the 10^{-5} s range if the radicals are generated in the proximity of a dropping mercury electrode by a pulse of high-energy radiation[1,2]. Depending upon the potential of the electrode either anodic or cathodic waves are registered which provide an insight into the redox behavior of the radicals. The carbonate radical ion is generated on irradiation of a 10^{-2} M aqueous Na_2CO_3 solution saturated with N_2O; the OH radicals produced by radiolysis of water immediately oxidize carbonate[3] according to:

$$OH + CO_3^{2-} \rightarrow OH^- + CO_3^-$$

At potentials < 0.25 V (*vs.* hydrogen electrode) cathodic waves are observed which rapidly decay (Fig. 1, bottom right) owing to electrochemical consumption of the radical according to equation (1).

$$CO_3^- + e^- \rightarrow CO_3^{2-} \qquad (1)$$

In solution CO_3^- has a lifetime of more than 1 ms, as revealed by the diminution of its absorption at 600 nm. For greater

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positive electrode potentials anodic waves are observed. The polarogram of CO_3^- measured 40 μs after its generation and depicted in Figure 1 shows that the transition from reduction according to equation (1) to oxidation according to equation (2) occurs within a relatively narrow voltage range. The theory

$$CO_3^- \rightarrow CO_3 + e^- \qquad (2)$$

of the polarography of free radicals[2] interprets this observation as indicating that the standard redox potential of the CO_3^-/CO_3^{2-} system is more positive than that of the CO_3/CO_3^- system.

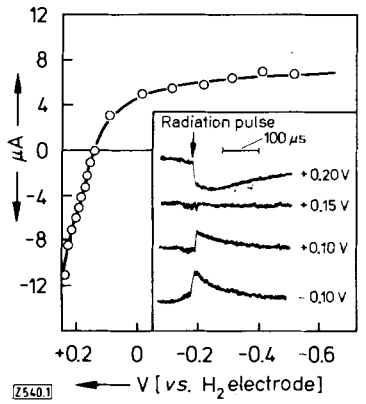

Fig. 1. Polarogram of the CO_3^- radical; cathodic waves positive, anodic waves negative. Bottom right: current-time plots for various electrode potentials.

CO_3^- can abstract an electron from numerous substances having a redox potential less than 1.0 V. On the other hand, transfer of an electron from CO_3^- to duroquinone has also been detected[4]; duroquinone has a standard redox potential for a one-electron transfer of −0.235 V[5]. The carbon trioxide CO_3 formed in this reaction decomposes to carbon dioxide and oxygen.

The ability of CO_3^- to function both as a one-electron donor and as a one-electron acceptor appears particularly interesting in connection with light-induced, carbonate-catalyzed decomposition of water to produce oxygen. As has recently been demonstrated[4, 6], triplet states of some quinones and nitro compounds oxidize CO_3^{2-} to CO_3^-. On the basis of these findings it is now possible to set up a photo-electrochemical half-cell for the production of O_2:

$$\begin{array}{lcl} & X \xrightarrow{h\nu} & X^* \\ X^* + CO_3^{2-} & \rightarrow & X^- + CO_3^- \\ CO_3^- + X & \rightarrow & X^- + CO_3 \\ CO_3 & \rightarrow & CO_2 + \tfrac{1}{2}O_2 \\ CO_2 + H_2O & \rightarrow & CO_3^{2-} + 2H^+ \\ \hline 2X + H_2O & \xrightarrow{h\nu} & 2X^- + 2H^+ + \tfrac{1}{2}O_2 \end{array}$$

The oxygen originates from the carbonate in the early stages of irradiation, as has also been postulated for the photosynthetic system[7].

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CAS Registry numbers:
CO_3^{2-}, 3812-32-6; CO_3^-, 16518-46-0

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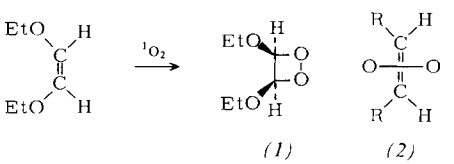
ABSTRACTS

1,2-Dioxetanes, which are formed by addition of singlet oxygen to CC double bonds, are dealt with by *P. D. Bartlett* in his "Ingold Lecture". Singlet oxygen is the only reagent capable of fast and stereospecific Diels-Alder reactions and [2+2]additions to CC double bonds. Such an addition is the formation of dioxetane *(1)* which could begin with an antarafacial approach of olefin and $^1O_2$ as shown in *(2)*. Thermal cleavage



(1) *(2)*

of 1,2-dioxetanes affords two carbonyl fragments, generally with chemiluminescence. [Four-membered Rings and Reaction Mechanisms. Chem. Soc. Rev. 5, 149—163 (1976); 41 references]

[Rd 879 IE—F]

The influence of isotopic substitution on diffusion in liquids is the subject of a report by *R. Mills* and *K. R. Harris.* Modification of the mass of a diffusing molecule and measurement of the resulting change in its mobility permits assessment of the influence of mass on the rate of diffusion. The rate of diffusion depends upon factors such as mass, shape, and interaction potentials. If the diffusing molecules are different then the influence of mass is usually masked. Most self-diffusion data can be explained in terms of classical theory. The change in mass has hardly any effect on the diffusion of tracers. [The Effect of Isotopic Substitution on Diffusion in Liquids. Chem. Soc. Rev. 5, 215—231 (1976); 52 references]

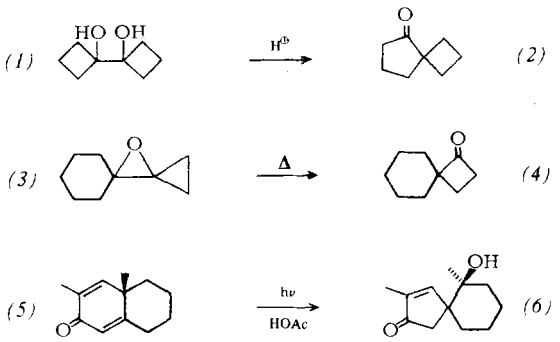
[Rd 881 IE—F]

Synthesis of fluoro-organic compounds by high-temperature conversion of saturated, unsaturated, aromatic, and heterocyclic fluorine compounds is treated in a review by *V. B. Platonov* and *G. G. Yakobson.* While the pyrolysis of perfluorinated paraffins affords complex mixtures partially fluorinated and fluoro halo compounds give fluorinated alkenes and arenes in high yields. The thermal conversion of perfluorocycloalkanes is strongly dependent upon ring size. Pyrolysis of polytetrafluoroethylene leads to perfluoroalkenes, -cycloalkenes, -alkanes, and -arenes, while perfluoroalkenes and -alkynes cyclize and perfluorocycloalkenes are transformed into perfluoroalkenes, -arenes, and condensation products. Thermolysis

of unsaturated compounds in the presence of difluorocarbene generators (difluorochloromethane, tetrafluoroethylene) furnishes high yields of fluorinated arenes which disproportionate and isomerize on heating. Homologs of perfluorinated arenes and heterocycles can be obtained by pyrolysis in the presence of difluorocarbene generators. [The Application of Thermolytic Reactions for the Syntheses of Fluoro-Organic Compounds. Synthesis *1976*, 374—384; 88 references]

[Rd 884 IE—M]

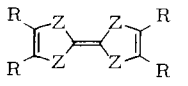
The synthesis of carbocyclic spiro compounds *via* rearrangement routes is reviewed by *A. P. Krapcho*. Acid-catalyzed reactions include, *inter alia*, pinacol rearrangements [*(1)*→*(2)*]; examples of thermal rearrangements are provided, *inter alia*, by the oxiranes [*(3)*→*(4)*] and alkenes. Spiro compounds



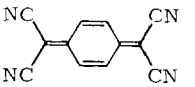
can also be obtained by photochemical excitation of cyclic cross-conjugated dienones and other compounds [*(5)*→*(6)*], as well as by other rearrangement processes such as reductions, solvolyses, and eliminations. [Synthesis of Carbocyclic Spiro Compounds *via* Rearrangement Routes. Synthesis *1976*, 425—444; 184 references]

[Rd 885 IE—M]

The synthesis of tetrathiafulvalenes *(1)* and tetraselenafulvalenes *(2)* is dealt with in an article by *M. Narita* and *C. U. Pittmann, Jr.* Compounds *(1)* are prepared, *inter alia*, by deprotonation of 1,3-dithiolylium ions and desulfurization of 2-thioxo-1,3-dithiols with P^{III} compounds. Compounds *(2)* are obtained analogously from 2-selenoxo-1,3-diselenols. *(1)*



(1), Z = S
(2), Z = Se



(3)

and *(2)* are of interest, primarily because they react with tetracyanoquinodimethane *(3)* and other electron acceptors to give charge transfer complexes which behave electrically and optically like unidimensional metals at room temperature. [Preparation of Tetrathiafulvalenes (TTF) and their Selenium Analogs—Tetraselenafulvalenes (TSeF). Synthesis *1976*, 489—514; 91 references]

[Rd 886 IE—M]

Reactions on single-crystal surfaces forms the subject of a review by *G. A. Somorjai*. Catalytic and other reactions on solid surfaces can be truly understood only if the elementary steps of surface chemical reactions are known. It has proven useful to combine studies of surface structure and composition with kinetic studies of reaction rate and reaction path. In the studies described, freshly cleaved metal single-crystals were used. Their surface was investigated before and after the reaction. The gas or gas mixture was directed onto the crystal surface in the form of a molecular beam, whose scattering and composition could be monitored. [Reactions on Single-Crystal Surfaces. Acc. Chem. Res. *9*, 248—256 (1976); 42 references]

[Rd 888 IE—L]

BOOK REVIEWS

The Theory of Molecular Spectroscopy. Vol. 1. The Quantum Mechanics and Group Theory of Vibrating and Rotating Molecules. By *C. J. H. Schutte*. North-Holland Publ. Co., Amsterdam 1976. 1st edit., 512 pp., numerous figs., bound, Hfl. 170.—/$ 67.95.

This work, planned for two volumes, is intended for scientists active in the field of rotational and rotation-vibrational spectroscopy and for interested advanced students.

The present first volume is divided into six chapters and an extensive appendix. In the first chapter (41 pages) a short section is provided that gives the mathematical basis essential for understanding subsequent parts of the book. Particular stress is laid on the treatment of linear vector space, on the theory of matrices, and on matrix representation of linear operators.

The second chapter (80 pages) contains a fundamental introduction to group theory and its applicability to molecular spectroscopy; two separate specialized sections of this chapter deal with the approaches to group-theoretical treatment of nonrigid molecules and with the prerequisites for application of group theory to the spectra of solids. The chapter is rounded off by three sections of the appendix that contain, *inter alia*, the character tables for 51 point groups, subgroups and supergroups, as well as correlation tables.

In the third chapter (66 pages) some quantum-mechanical principles are outlined: the subjects are not only the basic postulates and most important methods of calculation in quantum mechanics, but also details of harmonic and anharmonic oscillators, quantum mechanics of angular momentum, calculation of the hydrogen atom and the Pauli principle.

The fourth chapter (39 pages) is concerned with the exact, classical and quantum-mechanical Hamiltonian operator for vibrating and rotating molecules.

In the fifth chapter (73 pages) the Born-Oppenheimer approximation is presented for H_2^+ and the H_2 molecules. Further sections of this chapter deal with the matching experimental data and potential functions, with the quantum-mechanical virial theorem, and with theoretical approaches to the calculation of dipole moments and molecular polarizabilities.

The final chapter (81 pages) deals with the interaction of electromagnetic radiation and matter; semiclassical treatment of this problem is used to derive the selection rules for rotational and vibrational transitions in absorption spectra. The chapter concludes with a brief presentation of the theory of Raman spectroscopy.

Numerous textbooks are cited at the beginning of each chapter as a guide to further reading. A comprehensive index

facilitates the reader's search for individual problems. The chapters are well arranged as far as subject matter is concerned, but the WKB method that is mentioned several times in Chapter 5 really deserved a short introduction within the framework of the third chapter. A larger number of mathematical examples would enhance the value of the book.

Taken as a whole, this first volume can be regarded as successful because of its clear, easily readable, and concise presentation of the subject.

Rainer Moormann [NB 337 IE]

Kunststoff-Handbuch. Band 1, Grundlagen (Plastics Handbook. Vol. 1, Fundamentals). Edited by *R. Vieweg* and *D. Braun*. Carl Hanser Verlag, Munich-Vienna 1975. 1st Edit., xx, 1342 pp., 942 figs., 113 tables, linen, DM 595.—.

The eleven-volume Plastics Handbook is completed by the volume on "Fundamentals" that has now appeared[*]. Since the Handbook is intended to provide information on the possible uses of plastics not only for chemists and physicists but also for manufacturers, architects, electrical engineers, *etc.*, this "General" volume on the scientific and industrial basics of the plastics sector has long been anxiously awaited. Even though the editors emphasize that it was never their intention to provide a textbook of macromolecular chemistry and physics and of plastics technology, it must be recognized and noted that they have succeeded excellently in setting out, in clear and readily comprehensible form, the knowledge of fundamentals essential for the volumes on individual topics.

The basic principles of the chemistry and then the physics of plastics are treated in well-devised and clear sections, with much space devoted to measurements and test procedures. Particular mention may be made of a chapter in which the properties of plastics are compared with those of other materials. A further section treats the principles of plastics processing, *e.g.* their forming, joining, separation, and improvement, including the principles of mold construction and the various equipment for injection molding, extrusion presses, and blowers.

Finally, separate chapters deal with the principles of plastics standardization from a national and an international standpoint, with the economics of plastics and relevant statistics, and with organizations and research institutes.

Understanding of the specialist volumes will be found easier and deeper if the reader also consults the corresponding chapter in the "General" volume. It is a remarkable achievement to have coordinated the contributions of many authors into a compilation that can be understood even by the non-expert. For all those interested in a deeper insight the rich reference list at the end of each chapter provides a sufficient introduction into the original literature.

With this volume the Plastics Handbook receives its accolade as a complete work, for the good reviews, the instructive illustrations, and the good subject index simplify its use by all those interested in plastics. With this work, which has no equal in the world literature, the editors and the publisher have done a great service to the plastics sector. Both the "General" volume and the complete work can be recommended without any reservations as of great use to all who develop, manufacture, or use plastics.

Otto Horn [NB 339 IE]

Subnuclear Components. Preparation and Fractionation. Edited by *G. D. Birnie*. Butterworths, London 1976. 1st edit., 334 pp., numerous figs. and tables, bound, £ 15.00.

Following the successful introduction of "Subcellular Components" the appearance of "Subnuclear Components" provides another highly practical book from the same editor. *G. D. Birnie* has succeeded, together with a renowned group of research-experienced collaborators, in selecting and testing critically a large number of published methods for the isolation and fractionation of eukaryotic cell nuclei.

The individual sections provide, in clear arrangement, a wealth of experimental detail about the isolation of cell nuclei, cell membranes, nucleoli, chromatin, histones, non-histone proteins, and nuclear RNA and DNA. The advantages and disadvantages of the methods for special applications and difficulties arising therein are discussed in detail; criteria are announced that can be brought in to assess the chemical and biological quality of the preparations.

Analytical procedures for the characterization of the isolated structures or molecules naturally take up a large space in each chapter. Besides the electron-optical techniques and conventional methods such as the determination of enzyme activities or the amino-acid composition of proteins, less known methods are described, such as isopyknic centrifuging in metrizamide gradients or the isoelectric focussing of non-histone proteins.

It is made clear, particularly in the chapter on the isolation of chromatin, that experimental results obtained in the fractionation of the cell nucleus depend largely on the conditions used during the preparation and must be interpreted accordingly. It is thus very important that the reader obtains not only an introduction to the choice of methods for his own research but also indications on how to evaluate published data.

Anton Schweiger [NB 344 IE]

Vom Wasser, Vol. 46. Issued by the Fachgruppe Wasserchemie in der Gesellschaft Deutscher Chemiker. Responsible for the text: *W. Husmann*. Verlag Chemie, Weinheim 1976. 296, A 96 pp., bound, DM 88.00.

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[*] Cf. Angew. Chem. Int. Ed. Engl. *14*, 579 (1975).

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Catalyzed Addition of Aldehydes to Activated Double Bonds —A New Synthetic Approach

New synthetic methods (17)

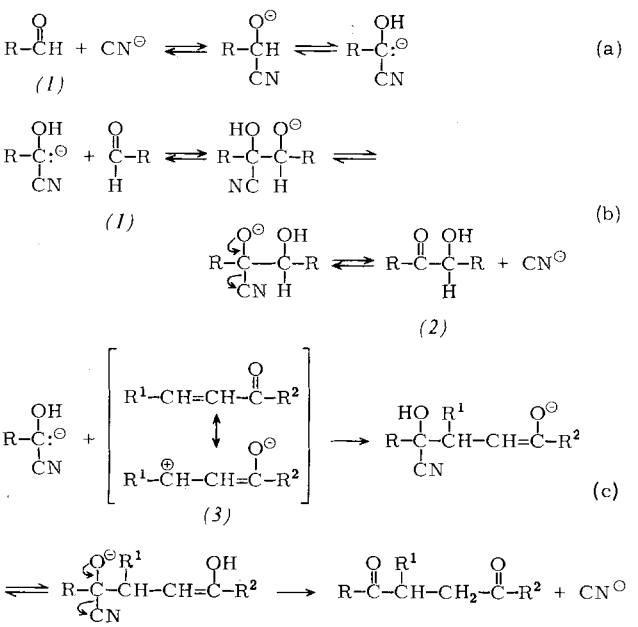
By Hermann Stetter[*]

In the presence of cyanide ions as catalyst, aromatic and heterocyclic aldehydes can be smoothly added to α,β-unsaturated ketones, esters, and nitriles in aprotic solvents to form γ-diketones, 4-oxo carboxylic esters, and 4-oxo nitriles. Thiazolium salts in the presence of bases are also suitable catalysts; they permit not only addition of aromatic and heterocyclic aldehydes but also the addition of aliphatic aldehydes.

1. General

One of the longest known reactions of organic chemistry is the benzoin condensation, in which aromatic and heterocyclic aldehydes *(1)* are transformed into acyloins (α-hydroxy ketones) *(2)*. Cyanide ions serve as catalysts. The reaction is reversible, and dependent upon the formation of a carbanion stabilized by the nitrile group. We found that this carbanion can be added to the double bond of α,β-unsaturated ketones, esters, and nitriles; an irreversible reaction then occurs to give γ-diketones, 4-oxo carboxylic esters, and 4-oxo nitriles[1].

The mechanism is formulated for the addition of aldehydes *(1)* to α,β-unsaturated carbonyl compounds *(3)*. Formation of benzoin *(2)* is reversible and kinetically controlled [eq. (a) to (c)].



It is essential that the reaction be carried out in aprotic solvents, general preference being given to dimethylformamide. Being a fast reversible reaction, benzoin formation [eq. (b)] precedes addition [eq. (c)]. Thus use of the respective benzoin instead of the aldehyde gives the same products. Between 0.1 and 0.5 equivalent of sodium or potassium cyanide serves as catalyst. The reaction time is generally 1 to 4 h at *ca.* 35 °C. Attempted reaction fails with aliphatic aldehydes because they preferentially undergo aldol condensation under the influence of the strongly alkaline cyanide salts. Addition of aliphatic aldehydes has been accomplished by the following route:

It is known from biochemistry that vitamin B_1 (thiamine) can convert aliphatic aldehydes into acyloins in buffered

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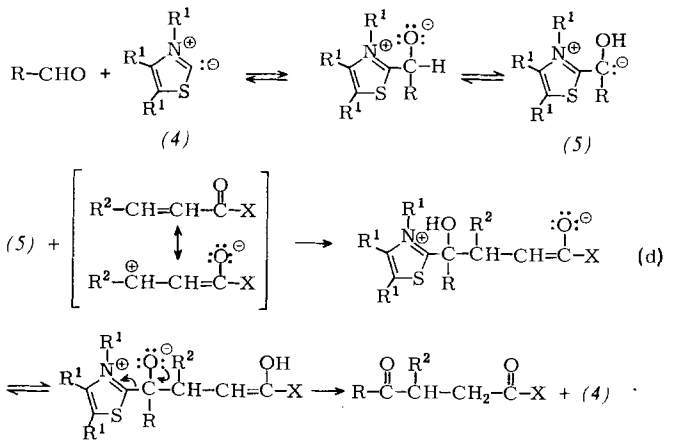
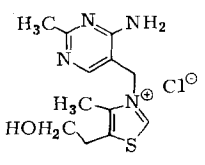
aqueous solutions[2]. The catalytic activity is associated with the thiazolium component of the vitamin. In the presence of bases, quaternary thiazolium salts are transformed into the ylide structure *(4)*, the ylide being able to exert a catalytic effect resembling that of the cyanide ion in benzoin condensation.

It is also known that thiazolium salts can in general assume this catalytic function. And similar observations have also been made with other azolium salts, *e.g.* benzimidazolium salts and benzo- and naphtho[2,1-*d*]thiazolium salts[2, 3]. We have successfully employed thiazolium salts in the presence of bases as catalysts for addition of aliphatic, and also aromatic and heterocyclic, aldehydes to α,β-unsaturated ketones, esters, and nitriles. Reactions yields γ-diketones, 4-oxo carboxylic esters, and 4-oxo nitriles, respectively [eq. (d)][4].

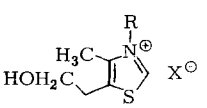


(d)

Extensive studies on quaternary thiazolium salts, *e.g.* 1,3-thiazole, 4,5-dimethyl-1,3-thiazole, and poly-4-methyl-5-vinyl-1,3-thiazole, and corresponding salts of other heterocycles, *e.g.* 1-methylbenzimidazole and 4-*p*-chlorophenyl-1,2,4-triazole demonstrated catalytic activity in nearly all the salts tested. However, since there seems to be no decisive advantage over the use of quaternary salts of 5-(2-hydroxyethyl)-4-methyl-1,3-thiazole only salts of this inexpensive, commercially available thiazole [Merck AG, Darmstadt (Germany)] were used. With aliphatic aldehydes, *N*-benzylated salts such as 3-benzyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium chloride (Cat. 1) proved most suitable, while aromatic aldehydes responded best to *N*-alkylated salts such as 3-ethyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium bromide (Cat. 2) or 5-(2-hydroxyethyl)-3,4-dimethylthiazolium iodide (Cat. 3)[20]. Both kinds of catalyst were suitable for heterocyclic aldehydes. (Tested procedures for making the catalysts are to be found at the end of this article.)



Thiamine



Cat. 1, R = $C_6H_5CH_2$, X = Cl
Cat. 2, R = C_2H_5, X = Br
Cat. 3, R = CH_3, X = I

The most suitable bases are triethylamine and sodium acetate. The amount of catalyst is usually 0.1 equivalent but can be reduced to 0.05 equivalent. Both protic solvents like alcohol and aprotic ones like dimethylformamide and dioxane may be considered. Working without solvent also has its advantages in many cases. Under nitrogen, reaction times of 6 to 15 h and temperatures of 60 to 80 °C are necessary. As in the case of cyanide catalysis, the benzoins can be used instead of the aromatic and heterocyclic aldehydes, since benzoin formation is once again the initial kinetically controlled reaction. Aliphatic aldehydes could not be replaced by the acyloins.

2. Production of γ-Diketones

2.1. By Addition of Aliphatic Aldehydes to α,β-Unsaturated Ketones

As already mentioned, the addition of aliphatic aldehydes to α,β-unsaturated ketones can only proceed on catalysis by azolium salts. The examples listed in Table 1 were carried out exclusively with Cat. 1. A large number of aliphatic aldehydes could be converted into γ-diketones by reaction with aliphatic, aromatic, and heterocyclic α,β-unsaturated ketones. Working without solvent was frequently advantageous.

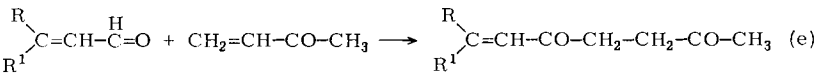
Table 1. γ-Diketones from aliphatic aldehydes and α,β-unsaturated ketones. Catalyst: Cat. 1.

$R-CHO + R^1-CH=CH-CO-R^2 \longrightarrow R-CO-CHR^1-CH_2-CO-R^2$

R	R^1	R^2	Solvent	Yield [%]	Ref.
CH_3	H	CH_3	None	61	[7, 8]
C_2H_5	H	CH_3	Ethanol	60	[7, 8]
n-C_3H_7	H	CH_3	Ethanol	68	[7, 8]
n-C_4H_9	H	CH_3	Ethanol	68	[7, 8]
n-C_5H_{11}	H	CH_3	Ethanol	68	[7, 8]
n-C_6H_{13}	H	CH_3	None	78	[5, 7]
n-C_7H_{15}	H	CH_3	Ethanol	70	[7, 8]
n-C_9H_{19}	H	CH_3	Ethanol	74	[7, 8]
n-C_9H_{19}	H	CH_3	None	88	[8]
n-$C_{11}H_{23}$	H	CH_3	Ethanol	76	[8]
$C_6H_5CH_2CH_2$	H	CH_3	Ethanol	61	[8]
$CH_3(CH_2)_2$—$CH(CH_3)$	H	CH_3	Ethanol	38	[8]
i-C_3H_7	H	CH_3	Ethanol	41	[8]
CH_3	C_6H_5	CH_3	Ethanol	20	[6]
n-C_3H_7	C_6H_5	CH_3	Ethanol	35	[6]
n-C_3H_7	C_6H_5	C_6H_5	Ethanol	70	[6]
$C_6H_5CH_2CH_2$	C_6H_5	C_6H_5	Ethanol	46	[6]
C_2H_5	2-Pyridyl	C_6H_5	Ethanol	65	[9]
CH_3	3-Pyridyl	C_6H_5	DMF	65	[9]
C_2H_5	3-Pyridyl	C_6H_5	Ethanol	75	[9]
n-C_3H_7	3-Pyridyl	C_6H_5	Ethanol	95	[9]
n-C_3H_7	2-Furyl	C_6H_5	None	92	[9]
n-C_3H_7	2-Furyl	C_6H_5	Ethanol	88	[9]
n-C_3H_7	3-Pyridyl	3-Pyridyl	Ethanol	84	[9]
n-C_3H_7	3-Pyridyl	3-Pyridyl	None	67	[9]
n-C_3H_7	C_6H_5	2-Furyl	DMF	91	[9]
n-C_3H_7	C_6H_5	3-Pyridyl	Ethanol	89	[9]
n-C_3H_7	2-Furyl	2-Furyl	None	84	[9]
n-C_3H_7	C_6H_5	2-Thienyl	Ethanol	77	[9]
n-C_3H_7	2-Furyl	3-Pyridyl	Ethanol	88	[9]

Unsaturated and substituted aliphatic aldehydes can be used with equal success in the reaction. α,β-Unsaturated aldehydes could be transformed in satisfactory yields only on working in solvents. The hardly known δ,ε-unsaturated γ-diketones are obtained as products [eq. (e)].

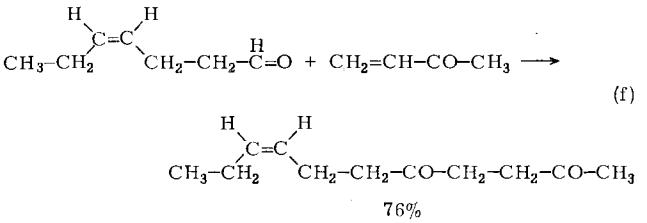
If the double bond is not conjugated with a carbonyl group then the addition can also be performed without solvent, as illustrated by the example of the preparation of *cis*-8-undecene-2,5-dione from *cis*-4-heptenal and butenone [eq. (f)][5].



(e)

$R = C_6H_5$, $R^1 = H$: 58%[7] $R = R^1 = C_6H_5$: 77%[7]

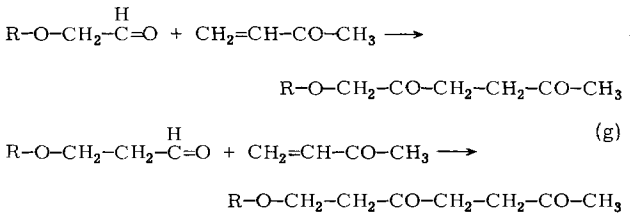
$R = R^1 = CH_3$: 52%[10] $R = (CH_3)_2C{=}CH{-}CH_2{-}CH_2$, $R^1 = CH_3$: 65%[11]



(f)

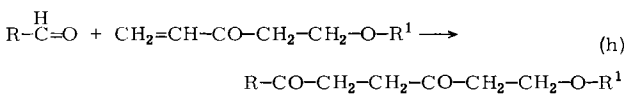
76%

A smooth reaction is also observed with aldehydes containing ether groups. Both ethers of glycolaldehyde and β-alkoxypropionaldehydes have been added to butenone. The δ-[12] and ε-alkoxy γ-diketones[10] could be obtained in 50—70% yield according to eq. (g).



(g)

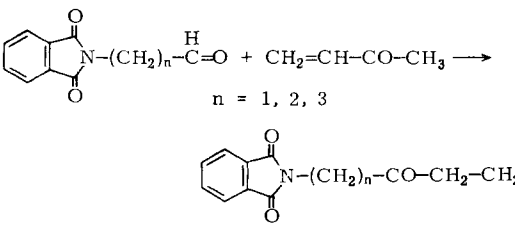
γ-Diketones containing ether groups are also obtained by addition of aldehydes to vinyl ketones bearing ether groups.



(h)

The addition of numerous aliphatic aldehydes according to eq. (h) has been accomplished in yields ranging around 80%[13].

Recent studies have shown that phthalimidoaldehydes can be added to butenone in yields of 66—75% [eq. (i)][14].



(i)

In the last-mentioned examples butenone was most commonly employed as unsaturated ketone. All the reactions can be performed with other unsaturated ketones, *e.g.* ethyl vinyl ketones, benzylideneacetone, and benzylideneacetophenone.

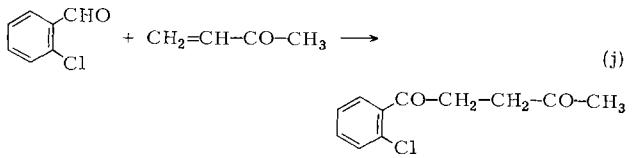
2.2. By Addition of Aromatic Aldehydes to α,β-Unsaturated Ketones

The most suitable technique for addition of aromatic aldehydes to α,β-unsaturated ketones utilizes cyanide catalysis in dimethylformamide as solvent. In practice, however, all the additions can also be accomplished with thiazolium salts as catalysts, preferably Cat. 2. Both unsubstituted aromatic aldehydes and those bearing substituents in the ring can add to aliphatic, aromatic, and heterocyclic α,β-unsaturated

Table 2. γ-Diketones from aromatic aldehydes and α,β-unsaturated ketones.

$R{-}CHO + R^1{-}CH{=}CH{-}CO{-}R^2 \longrightarrow R{-}CO{-}CHR^1{-}CH_2{-}CO{-}R^2$

R	R^1	R^2	Catalyst	Solvent	Yield [%]	Ref.
C_6H_5	H	CH_3	CN^-	DMF	82	[15]
C_6H_5	H	CH_3	Cat. 2	None	65	[6]
C_6H_5	H	C_2H_5	Cat. 2	DMF	62	[16]
C_6H_5	C_6H_5	CH_3	CN^-	DMF	80	[15]
C_6H_5	C_6H_5	C_6H_5	CN^-	DMF	93	[15]
C_6H_5	C_6H_5	C_6H_5	Cat. 2	Ethanol	84	[6]
C_6H_5	2-Furyl	C_6H_5	CN^-	DMF	73	[9]
C_6H_5	2-Furyl	C_6H_5	Cat. 3	Ethanol	86	[9]
C_6H_5	2-Furyl	2-Furyl	Cat. 3	Ethanol	82	[9]
C_6H_5	3-Pyridyl	2-Furyl	Cat. 3	Ethanol	65	[9]
C_6H_5	3-Pyridyl	C_6H_5	CN^-	DMF	87	[9]
C_6H_5	C_6H_5	3-Pyridyl	Cat. 3	Ethanol	80	[9]
C_6H_5	3-Pyridyl	3-Pyridyl	CN^-	DMF	48	[9]
C_6H_5	C_6H_5	2-Thienyl	CN^-	DMF	75	[9]
C_6H_5	2-Pyridyl	C_6H_5	Cat. 2	Ethanol	86	[9]
o-ClC_6H_4	H	CH_3	Cat. 2	None	56	[11]
o-$CH_3C_6H_4$	H	CH_3	Cat. 2	DMF	68	[16]
o-$CH_3C_6H_4$	H	C_2H_5	Cat. 2	DMF	70	[16]
o-$CH_3C_6H_4$	H	C_6H_5	Cat. 2	DMF	70	[16]
p-ClC_6H_4	H	CH_3	CN^-	DMF	98	[15]
p-ClC_6H_4	C_6H_5	CH_3	CN^-	DMF	98	[15]
p-ClC_6H_4	C_6H_5	C_6H_5	CN^-	DMF	98	[15]
p-$CH_3OC_6H_4$	H	CH_3	Cat. 2	Ethanol	42	[8]
o-$CH_3OC_6H_4$	H	C_2H_5	Cat. 2	DMF	53	[16]
o-$CH_3OC_6H_4$	H	C_6H_5	Cat. 2	DMF	75	[16]
3,4-$(OCH_2O)C_6H_3$	H	CH_3	Cat. 2	None	40	[8]
1-Naphthyl	H	CH_3	Cat. 2	DMF	58	[16]
1-Naphthyl	H	C_2H_5	Cat. 2	DMF	58	[16]
1-Naphthyl	H	C_6H_5	Cat. 2	DMF	79	[16]



(j)

ketones. *ortho*-Substituted benzaldehydes, which do not react on cyanide catalysis, represent an exception. In such cases satisfactory results are obtained on catalysis with thiazolium salts if vinyl ketones are co-reactants. For example, thiazolium salt-catalyzed reaction of 2-chlorobenzaldehyde with butenone affords the adduct in 56 % yield, while no reaction is observed on cyanide catalyst [eq. (j)][11].

Catalysis by thiazolium salts also gives better results with alkoxy aldehydes, whereas cyanide catalysis frequently fails (Table 2).

2.3. By Addition of Heterocyclic Aldehydes to α,β-Unsaturated Ketones

As with aromatic aldehydes, addition of heterocyclic aldehydes can be catalyzed by cyanide or thiazolium salt (Table 3). Cyanide catalysis is generally preferable; however, in some cases satisfactory results are obtained only on catalysis with thiazolium salts. Thus 2-pyridinecarbaldehyde still undergoes smooth addition to benzylideneacetophenone on cyanide catalysis, but good results are obtained only on thiazolium salt catalysis with other unsaturated ketones such as butenone. The reason probably lies in the specific structure of 2-pyridoin, which is stabilized by hydrogen bonding and therefore hinders the reverse reaction required on cyanide catalysis [cf. eq. (b)].

With furfural too, thiazolium salt catalysis can often be advantageous since the reaction products are obtained directly in high purity whereas formation of resinous products can interfere with work-up in the case of cyanide catalysis (Table 3).

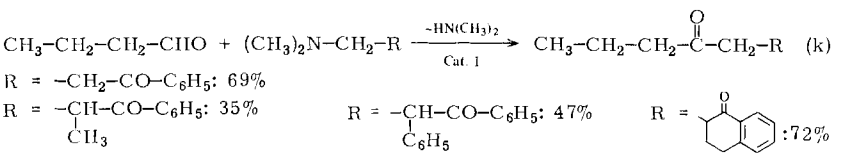
Table 3. γ-Diketones from heterocyclic aldehydes and α,β-unsaturated ketones.

$R-CHO + R^1-CH=CH-CO-R^2 \longrightarrow R-CO-CHR^1-CH_2-CO-R^2$

R	R^1	R^2	Catalyst	Solvent	Yield [%]	Ref.
2-Furyl	H	CH_3	Cat.1	Ethanol	80	[8]
2-Furyl	CH_3	CH_3	Cat.2	Ethanol	34	[6]
2-Furyl	C_6H_5	CH_3	Cat.2	Ethanol	80	[6]
2-Furyl	C_6H_5	CH_3	CN^-	DMF	72	[15]
2-Furyl	C_6H_5	C_6H_5	CN^-	DMF	93	[15, 18]
2-Furyl	C_6H_5	C_6H_5	Cat.2	Ethanol	91	[6]
2-Furyl	2-Furyl	C_6H_5	CN^-	DMF	61	[9]
2-Furyl	2-Furyl	2-Furyl	CN^-	DMF	45	[9]
2-Thienyl	H	CH_3	CN^-	DMF	80	[17]
2-Thienyl	C_6H_5	CH_3	CN^-	DMF	77	[17]
2-Thienyl	C_6H_5	C_6H_5	CN^-	DMF	90	[17]
2-Thienyl	C_6H_5	2-Thienyl	CN^-	DMF	80	[17]
2-Pyridyl	H	CH_3	Cat.3	Dioxane	75	[9]
2-Pyridyl	H	C_2H_5	Cat.3	Dioxane	65	[9]
2-Pyridyl	H	C_6H_5	Cat.3	Dioxane	76	[9]
2-Pyridyl	C_6H_5	CH_3	Cat.3	Dioxane	45	[9]
2-Pyridyl	C_6H_5	C_6H_5	CN^-	DMF	91	[15, 18]
3-Pyridyl	H	CH_3	CN^-	DMF	88	[15]
3-Pyridyl	H	C_6H_5	CN^-	DMF	80	[15]
3-Pyridyl	C_6H_5	2-Furyl	CN^-	DMF	80	[9]
3-Pyridyl	2-Furyl	C_6H_5	CN^-	DMF	73	[9]
3-Pyridyl	2-Furyl	2-Furyl	CN^-	DMF	88	[9]
3-Pyridyl	3-Pyridyl	2-Furyl	Cat.3	Ethanol	66	[9]
3-Pyridyl	3-Pyridyl	C_6H_5	CN^-	DMF	83	[9]
3-Pyridyl	C_6H_5	3-Pyridyl	Cat.3	None	76	[9]
3-Pyridyl	C_6H_5	3-Pyridyl	CN^-	DMF	72	[9]
3-Pyridyl	3-Pyridyl	3-Pyridyl	CN^-	DMF	74	[9]
4-Pyridyl	H	CH_3	CN^-	DMF	70	[15]

2.4. By Addition of Aldehydes with Application of Mannich Bases

In the Michael addition, Mannich bases can often be used in place of α,β-unsaturated ketones. The reaction then proceeds *via* an elimination-addition mechanism. We found that the α,β-unsaturated ketones can also be replaced by Mannich bases in the catalyzed addition of aldehydes. The aliphatic aldehydes could react with Mannich bases on catalysis with thiazolium salts. The best results were obtained on working in dimethylformamide at 80 to 90 °C. Examples are shown in eq. (k)[19].



(k)

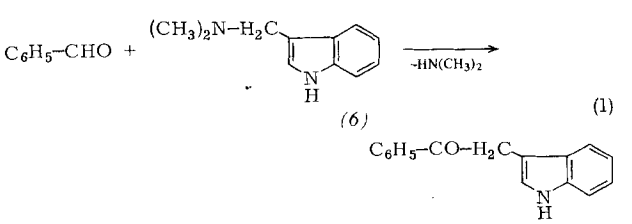
Aromatic and heterocyclic aldehydes can also be cleanly added to Mannich bases in cyanide-catalyzed reaction to give γ-diketones on working at 35 to 100 °C in dimethylformamide. Table 4 surveys the reactions with benzaldehyde.

Table 4. γ-Diketones from benzaldehyde and Mannich bases [19].

$C_6H_5-CHO + (CH_3)_2N-CH_2-CHR^1-CO-R^2 \longrightarrow C_6H_5-CO-CH_2-CHR^1-CO-R^2$

R^1	R^2	T [°C]	Yield [%]
H	CH_3	40	47
H	i-C_3H_7	70	60
$-(CH_2)_4-$		40	10
H	C_6H_5	35	64
CH_3	C_6H_5	100	49
C_6H_5	C_6H_5	40	58
		40	63

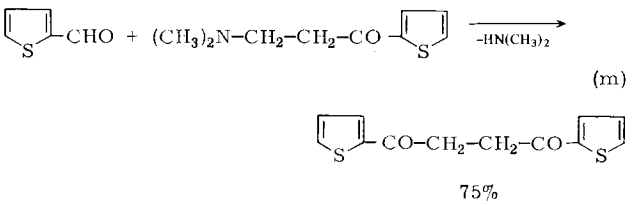
The alkaloid gramin *(6)*, which is readily accessible by Mannich reaction from indole, formaldehyde, and dimethylamine, also reacts with benzaldehyde in the presence of a cyanide catalyst to give a 52 % yield of ω-(3-indolyl)acetophenone [eq. (l)][19].



(l)

Examples for the use of heterocyclic aldehydes are the reactions of 3-pyridinecarbaldehyde with 3-dimethylamino-1-

phenyl-1-propanone[18] (35%), of furfural with 3-dimethylamino-1-(2-furyl)-1-propanone[4], and of 2-thiophenecarbaldehyde with 3-dimethylamino-1-(2-thienyl)-1-propanone [eq. (m)][17].

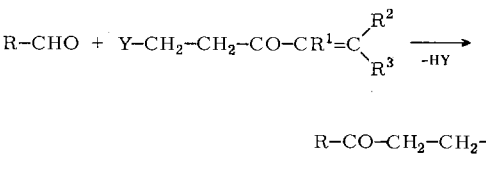


(m)

75%

Particular interest attaches to the use of Mannich bases of unsaturated ketones, which leads to unsaturated γ-diketones of the same type as are obtained on addition of α,β-unsaturated aldehydes when catalyzed by thiazolium salts [see eq. (e)]. In some cases it proved necessary to use the methylammonium iodide instead of the simple Mannich base (Table 5).

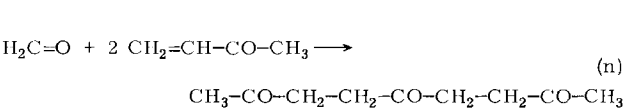
Table 5. γ-Diketones from aldehydes and Mannich bases. Catalyst: thiazolium salts [19].



R	Y	R^1	R^2	R^3	Yield [%]
CH_3	$N(CH_3)_3^+I^-$	H	CH_3	CH_3	23
n-C_3H_7	$N(CH_3)_2$	H	CH_3	CH_3	53
$(CH_3)_2C{=}CH$	$N(CH_3)_3^+I^-$	H	CH_3	CH_3	16
C_6H_5	$N(CH_3)_3^+I^-$	H	CH_3	CH_3	55
2-Thienyl	$N(CH_3)_3^+I^-$	H	CH_3	CH_3	45
n-C_3H_7	$N(CH_3)_2$	CH_3	CH_3	H	41
n-C_3H_7	$N(CH_3)_2$	$-(CH_2)_3-$		H	48
n-C_3H_7	$N(CH_3)_2$	$-(CH_2)_4-$		H	61
C_6H_5	$N(CH_3)_2$	$-(CH_2)_4-$		H	25

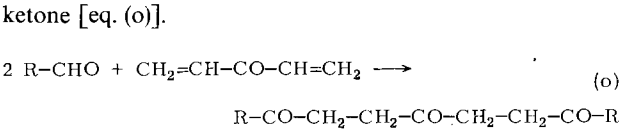
3. Preparation of Tri- and Polyketones

Addition of formaldehyde to butenone catalyzed by thiazolium salts gives 2,5,8-nonanetrione in 27% yield[7, 8].



(n)

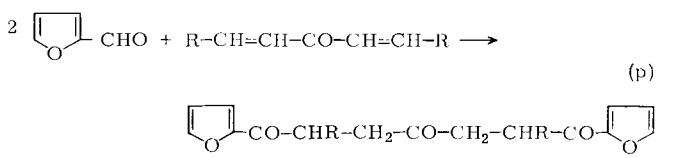
Such 1,4,7-triketones can be obtained much more readily by thiazolium salt-catalyzed addition of aldehydes to divinyl ketone [eq. (o)].



(o)

With aliphatic aldehydes the best results are achieved on working without solvent, whereas working in dimethylformamide is preferred with aromatic and heterocyclic aldehydes. The following aldehydes were transformed by divinyl ketone into the triketones[20]: acetaldehyde (70% yield), propanal (60%), *n*-butanal (65%), *i*-butanal (62%), *n*-pentanal (62%), *n*-hexanal (65%), *n*-heptanal (64%), *n*-octanal (66%), *n*-decanol (63%), benzaldehyde (55%), *p*-chlorobenzaldehyde (60%), *p*-methoxybenzaldehyde (30%), furfural (50%), and 2-thiophenecarbaldehyde (51%).

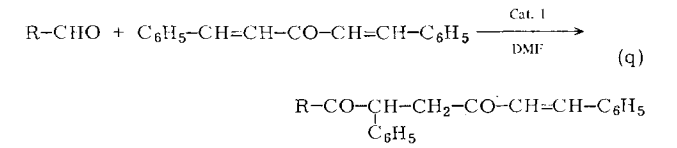
Furfural could be smoothly added to dibenzylideneacetone and difurfurylideneacetone, giving the triketones [eq. (p)][20].



(p)

R = C_6H_5: 54%; R = 2-Furyl: 44%

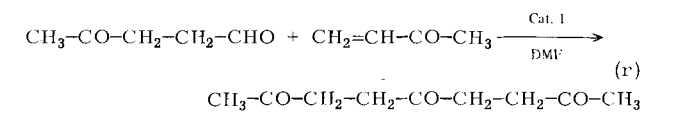
Interestingly, the addition of aliphatic aldehydes could only be accomplished in the ratio 1:1 [eq. (q)], the products being unsaturated γ-diketones[20].



(q)

R = CH_3: 85%; R = C_2H_5: 72%; R = n-C_4H_9: 65%

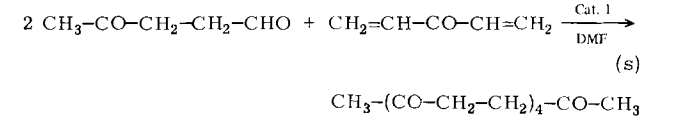
The addition of levulinaldehyde to α,β-unsaturated ketones leads according to eq. (r) to 1,4,7-triketones[20].



(r)

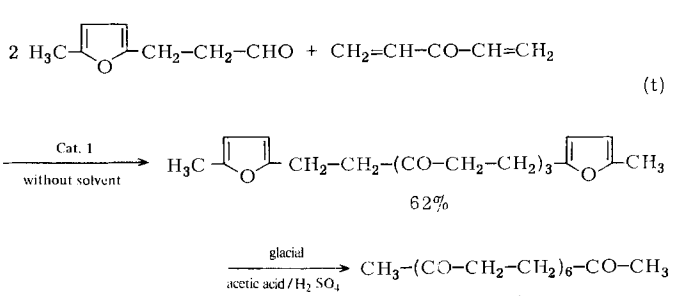
60%

If 2 mol of levulinaldehyde is allowed to act upon 1 mol of divinyl ketone then 2,5,8,11,14-pentadecanepentone is obtained in 40% yield [eq. (s)][20].



(s)

In one case a heptaketone, 2,5,8,11,14,17,20-heneicosaneheptone, could be obtained according to eq. (t). The preparation consisted in addition of 3-(5-methyl-2-furyl)propanal to divinyl ketone in the ratio 2:1 followed by hydrolysis of the adduct[20].

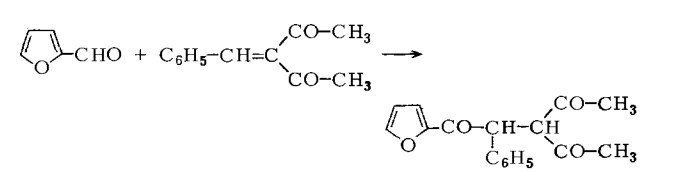


(t)

62%

70%

The thiazolium salt-catalyzed addition of aldehydes to alkylidene- or arylidene-β-diketones leads to branched triketones. Thus, for example, addition of furfural to benzylideneacetylace-



tone in ethanol as solvent affords 3-acetyl-1-(2-furyl)-2-phenylpentane-1,4-dione in 63% yield[20a].

A pathway to tetraketones leads *via* addition of dialdehydes to α,β-unsaturated ketones. Addition occurs only on catalysis with thiazolium salts, both for aliphatic and for aromatic and heterocyclic aldehydes. The yields of tetraketones generally remain below 50% (Table 6).

Table 6. Tetraketones from dialdehydes and butenone [20].

$$OHC\text{-}X\text{-}CHO + 2\ CH_2{=}CH\text{-}CO\text{-}CH_3 \longrightarrow CH_3\text{-}CO\text{-}CH_2\text{-}CH_2\text{-}CO\text{-}X\text{-}CO\text{-}CH_2\text{-}CH_2\text{-}CO\text{-}CH_3$$

X	Catalyst	Solvent	Yield [%]
$-(CH_2)_2-$	Cat. 1	DMF	43
$-(CH_2)_3-$	Cat. 1	DMF	33
$-(CH_2)_4-$	Cat. 1	DMF	7
$-(CH_2)_6-$	Cat. 1	DMF	46
$-(CH_2)_8-$	Cat. 1	DMF	48
m-C_6H_4	Cat. 3	Ethanol	21
p-C_6H_4	Cat. 3	Ethanol	29

4. Production of Dioxo Carboxylic Esters

Succinaldehydic methyl ester could be added to a series of vinyl ketones according to eq. (u), giving 4,7-dioxo carboxylic ester[21].

$$CH_3OOC\text{-}CH_2\text{-}CH_2\text{-}CHO + CH_2{=}CH\text{-}CO\text{-}R \xrightarrow[\text{Dioxane}]{\text{Cat. 1}} CH_3OOC\text{-}CH_2\text{-}CH_2\text{-}CO\text{-}CH_2\text{-}CH_2\text{-}CO\text{-}R \quad (u)$$

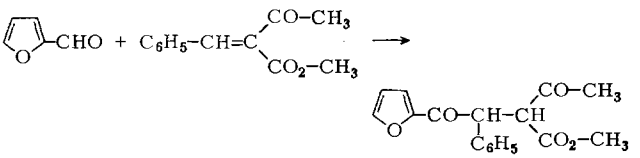
R = *n*-Pentyl: 64%; R = *n*-Hexyl: 69%; R = *n*-Heptyl: 71%; R = *n*-Octyl: 69%

Esters of this type are also obtained by adding aldehydes according to eq. (v) under the same conditions to methyl 4-oxohexenoate[22].

$$R\text{-}CHO + CH_2{=}CH\text{-}CO\text{-}CH_2\text{-}CH_2\text{-}COOCH_3 \longrightarrow R\text{-}CO\text{-}CH_2\text{-}CH_2\text{-}CO\text{-}CH_2\text{-}CH_2\text{-}COOCH_3 \quad (v)$$

R = Ethyl: 50%; R = *n*-Propyl: 52%; R = *n*-Butyl: 61%; R = *n*-Pentyl: 57%; R = *n*-Hexyl: 55%; R = *n*-Heptyl: 54%

Branched diketo carboxylic esters are obtained by thiazolium salt-catalyzed addition of aldehyde to alkylidene- or arylidene-β-keto carboxylic esters. Thus addition of furfural to the methyl ester of benzylideneacetoacetic acid in dioxane as solvent yields 1-(2-furyl)-3-methoxycarbonyl-2-phenylpentane-1,4-dione in 75% yield[20a].



5. Production of 4-Oxo Nitriles

Aromatic and heterocyclic aldehydes can be added extremely smoothly to α,β-unsaturated nitriles if the reaction is subjected to cyanide catalysis; high yields of 4-oxo nitriles are obtained [eq. (a) and (w)].

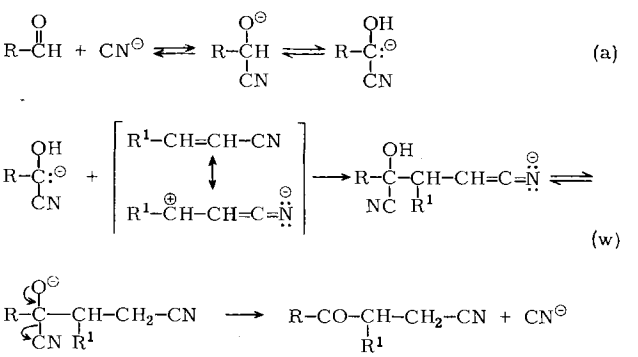


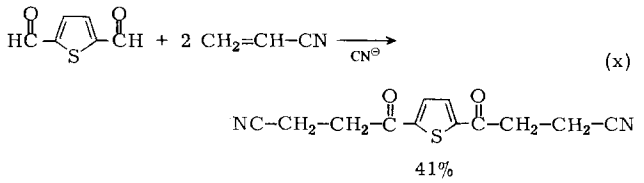
Table 7. 4-Oxo nitriles from aldehydes and α,β-unsaturated nitriles.

$$R\text{-}CHO + R^1\text{-}CH{=}CR^2\text{-}CN \longrightarrow R\text{-}CO\text{-}CHR^1\text{-}CHR^2\text{-}CN$$

R	R^1	R^2	Catalyst	Solvent	Yield [%]	Ref.
CH_3	H	H	Cat. 1	Ethanol	30	[6]
$(CH_3)_2C{=}CH$	H	H	Cat. 1	Ethanol	34	[23]
C_6H_5	H	H	CN^-	DMF	80	[1, 24]
C_6H_5	H	H	Cat. 1	DMF	52	[25]
C_6H_5	H	CH_3	CN^-	DMF	73	[24]
C_6H_5	CH_3	H	CN^-	DMF	71	[24]
C_6H_5	C_6H_5	H	CN^-	DMF	80	[24]
p-ClC_6H_4	H	H	CN^-	DMF	91	[24]
p-BrC_6H_4	H	H	CN^-	DMF	81	[24]
m-$CH_3C_6H_4$	H	H	CN^-	DMF	47	[26]
p-$CH_3C_6H_4$	H	H	CN^-	DMF	43	[26]
m-$CH_3OC_6H_4$	H	H	CN^-	DMF	83	[26]
p-$CH_3OC_6H_4$	H	H	CN^-	DMF	39	[26]
2-Naphthyl	H	H	CN^-	DMF	81	[26]
2-Furyl	H	H	CN^-	DMF	65	[18, 24, 27]
2-Furyl	H	H	Cat. 1	Ethanol	49	[6]
2-Furyl	CH_3	H	CN^-	DMF	73	[27]
2-Furyl	H	CH_3	CN^-	DMF	62	[27]
2-Furyl	C_6H_5	H	CN^-	DMF	68	[27]
2-Thienyl	H	H	CN^-	DMF	85	[18, 24]
2-Thienyl	CH_3	H	CN^-	DMF	76	[17]
2-Thienyl	C_6H_5	H	CN^-	DMF	71	[17]
5-Methyl-2-thienyl	H	H	CN^-	DMF	60	[17]
3-Pyridyl	H	H	CN^-	DMF	89	[18, 24]
4-Pyridyl	H	H	CN^-	DMF	71	[18, 24]

Dimethylformamide was found to be the best solvent. Sodium cyanide is required in amounts between 0.1 and 0.5 mol per mol of aldehyde. Aliphatic aldehydes can only be added to α,β-unsaturated nitriles on catalysis by thiazolium salts; aromatic and heterocyclic aldehyde also reacts under those conditions. In contrast to cyanide catalysis, however, satisfactory results are obtained only with acrylonitrile (Table 7).

Dialdehydes such as 2,5-thiophenedicarbaldehyde can also be added to acrylonitrile in the presence of cyanide ions [eq. (x)][17].



(x)

41%

6. Production of 4-Oxo Carboxylic Esters

In the presence of cyanide ions as catalyst, aromatic and heterocyclic aldehydes add to α,β-unsaturated carboxylic esters, forming 4-oxo carboxylic esters. The most suitable solvent is dimethylformamide, and the amount of catalyst is generally 0.1—0.5 equivalent. High-boiling oils which were not further characterized appeared as by-products. They are probably esters of acyloins also present in equilibrium. It is known that cyanide ions are excellent transesterification catalysts.

This transesterification can be suppressed by variation of the ester component. The yields admittedly increase on going from the methyl, *via* the ethyl and the isopropyl, to the *tert*-butyl esters; however, even on use of *tert*-butyl esters it was not possible to completely avoid side reactions. Overall, the cyanide-catalyzed addition of aldehydes to α,β-unsaturated esters is less favorable than the corresponding additions to α,β-unsaturated nitriles and ketones.

Both aliphatic and heterocyclic aldehydes undergo thiazolium-catalyzed addition to acrylic esters; however, the yields are not entirely satisfactory (Table 8).

Table 8. γ-Oxo carboxylic esters from aldehydes and α,β-unsaturated esters.

$R-CHO + R^1-CH=CR^2-COOR^3 \rightarrow R-CO-CHR^1-CHR^2-COOR^3$

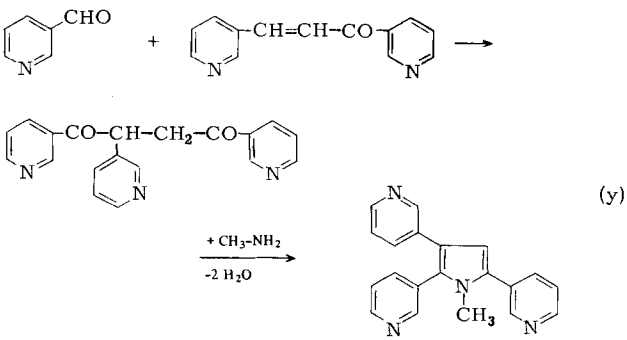
R	R^1	R^2	R^3	Catalyst	Yield [%]	Ref.
n-C_3H_7	H	H	C_2H_5	Cat. 1	29	[22]
C_6H_5	H	H	C_2H_5	CN^-	55	[28]
C_6H_5	CH_3	H	C_2H_5	CN^-	33	[1, 28]
C_6H_5	CH_3	H	i-C_3H_7	CN^-	40	[28]
C_6H_5	CH_3	H	t-C_4H_9	CN^-	52	[28]
p-ClC_6H_5	H	H	C_2H_5	CN^-	68	[28]
p-ClC_6H_5	CH_3	H	CH_3	CN^-	35	[28]
p-Cl_4H_4	CH_3	H	C_2H_5	CN^-	42	[1, 28]
p-ClC_6H_4	CH_3	H	i-C_3H_7	CN^-	49	[28]
p-ClC_6H_4	CH_3	H	t-C_4H_9	CN^-	64	[28]
p-ClC_6H_4	C_6H_5	H	C_2H_5	CN^-	54	[28]
p-ClC_6H_4	C_6H_5	H	t-C_4H_9	CN^-	60	[28]
p-ClC_6H_4	H	CH_3	CH_3	CN^-	34	[28]
2-Furyl	H	H	C_2H_5	Cat. 1	31	[4, 6]
2-Thienyl	H	H	C_2H_5	CN^-	50	[28]
2-Thienyl	CH_3	H	C_2H_5	CN^-	54	[28]
3-Pyridyl	H	H	C_2H_5	CN^-	37	[28]

7. Significance of the New Synthetic Approach

The synthetic approach described in this article is characterized by exceptional versatility, simplicity of operation, and high yields. The procedure is superior to most reactions for the synthesis of γ-diketones, 4-oxo nitriles, and 4-oxo carboxylic esters by virtue of its purely catalytic nature. The compounds produced are highly important intermediates of synthetic organic chemistry.

Starting from γ-diketones, it is very easy to prepare furans, pyrroles, thiophenes, and pyridazines. Most of the newly prepared diketones were characterized as the *N*-phenylpyrroles.

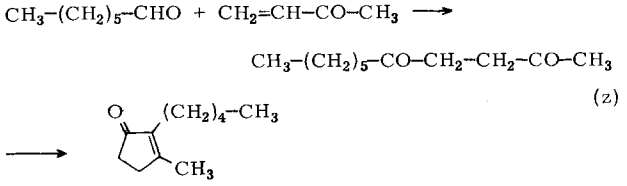
The versatility of this simple procedure can be illustrated for the synthesis of *N*-methyl-2,3,5-tri(3-pyridyl)pyrrole[9] [eq. (y)].



(y)

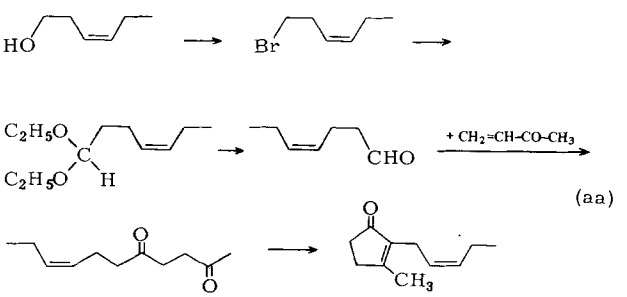
The possibility of obtained derivatives of cyclopentenone starting from γ-diketones by cyclizing aldol condensation is of particular interest. Many of the γ-diketones obtained were converted into cyclopentenones. Since numerous natural products, such as jasmine odors, prostaglandins, and pyrethrolone contain the cyclopentenone ring as structural unit, or can be derived therefrom, the reaction becomes particularly important.

In order to prepare the odiferous substance dihydrojasmone, 2,5-undecanedione [accessible in 80% yield by addition of *n*-heptanal to butenone] was subjected to cyclizing aldol condensation [eq. (z)][5].



(z)

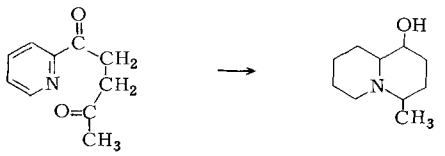
cis-Jasmone, which is also an odiferous substance, was produced according to eq. (aa) from *cis*-3-hexen-1-ol (leaf alcohol), which was converted into 1-bromo-*cis*-3-hexene and its Grignard compound. On treatment with diethyl phenylorthoformate the Grignard compound gave 7,7-diethoxy-*cis*-3-hep-



(aa)

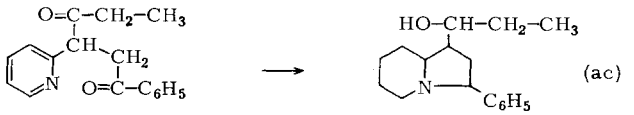
tene which could be converted into *cis*-4-heptenal with formic acid. The *cis*-8-undecene-2,5-dione resulting from addition of butenone furnished natural *cis*-jasmone by cyclizing aldol condensation[5]. The key step is addition of the aldehyde which can also be prepared by another pathway.

The γ-diketones readily accessible by addition of 2-pyridinecarbaldehyde to α,β-unsaturated ketones open up a facile entry to quinolizidines. Thus 4-methyl-1-quinolizidinol could be prepared in 75 % yield from 1-(2-pyridyl)-1,4-pentanedione by hydrogenation with platinum oxide in glacial acetic acid[9].



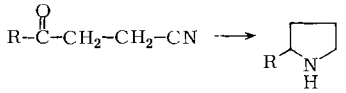
(ab)

Analogous hydrogenation of 1-phenyl-3-(2-pyridyl)-1,4-hexanedione likewise accessible *via* our reaction, which gives 1-(3-phenyl-1-indolizidinyl)-1-propanol according to eq. (ac) in 87 % yield[9], leads into the indolizidine series.



(ac)

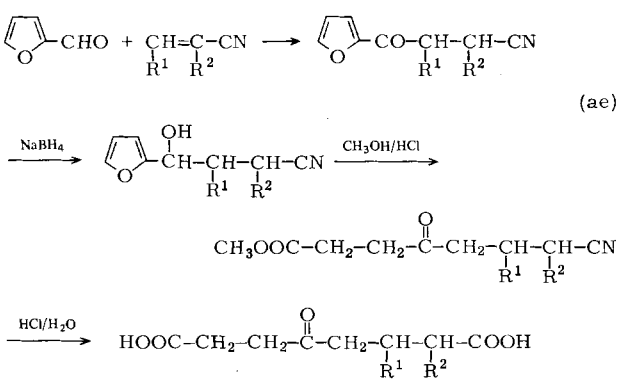
Numerous 4-oxo nitriles and their reaction products are also accessible by the aldehyde addition described. Catalytic hydrogenation to give pyrrolidines [eq. (ad)] is an important reaction.



(ad)

Among the numerous ring closures[29], special mention should be made of the facile nicotine synthesis utilizing the 4-oxo nitrile readily obtained in 80 % yield by addition of 3-pyridinecarbaldehyde to acrylonitrile[30].

The 4-oxo nitriles easily produced by addition of furfural to α,β-unsaturated nitriles according to eq. (ae) can be reduced by sodium tetrahydridoborate to form 4-hydroxy nitriles, which can be converted by Marckwald cleavage and hydrolysis into 4-oxooctanedioic acids. It is not necessary to isolate the intermediates[27].

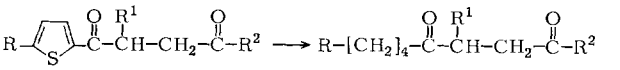


(ae)

$R^1 = R^2 = H$; $R^1 = CH_3$, $R^2 = H$; $R^1 = H$, $R^2 = CH_3$; $R^1 = C_6H_5$, $R^2 = H$

The γ-diketones and 4-oxo nitriles readily accessible by addition of thiophenecarbaldehydes could be converted by desulfurizing ring cleavage into aliphatic γ-diketones and 4-oxo carboxylic acids. The best results were obtained on desulfuration by Raney nickel in ethyl methyl ketone (Table 9)[17].

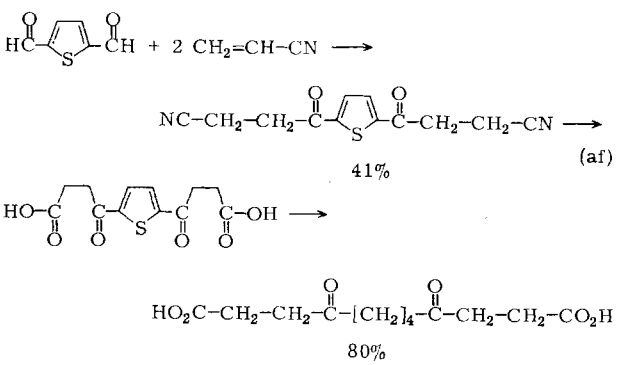
Table 9. γ-Diketones and 4-oxo carboxylic acids from thiophene derivatives [17].



R	R^1	R^2	Yield [%]
H	H	CH_3	60
H	C_6H_5	CH_3	77
H	C_6H_5	C_6H_5	75
H	C_6H_5	2-Thienyl [a]	58
H	H	2-Thienyl [a]	51
H	H	OH	77
H	CH_3	OH	83
H	C_6H_5	OH	78
CH_3	H	OH	79

[a] After reaction $R^2 = n$-butyl.

4,9-Dioxododecanedioic acid was prepared from 2,5-thiophenedicarbaldehyde according to eq. (af) [see eq. (x)][17].



(af)

The brief selection of examples presented above should provide an indication of the suitability of the compounds obtained as starting materials for other reactions. However, in view of the sheer volume of possibilities all such indications can only remain fragmentary.

8. Experimental

3-Benzyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium chloride (Cat. 1)[5]

5-(2-Hydroxyethyl)-4-methyl-1,3-thiazole (143.2 g, 1 mol; commercial product, *ex.* Merck AG, Darmstadt), freshly distilled benzyl chloride (126.6 g, 1 mol), and dry acetonitrile (500 ml) are mixed together in a 1000-ml three-necked flask fitted with a stirrer, a reflux condenser, and a stopper. The mixture is heated for 24 h under reflux and then allowed to cool to room temperature with constant stirring. (The product precipitates from the boiling solution on seeding after 12 h.) The product is isolated by vacuum filtration, washed colorless, subjected to preliminary drying, and then dried with gentle turning in a water-pump vacuum (bath temperature 90 °C). Yield 220.8 g (82%), m.p. 140–140.5 °C.

3-Ethyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium bromide (Cat. 2)[6]

5-(2-Hydroxyethyl)-4-methyl-1,3-thiazole (143.2 g, 1 mol), bromoethane (109.0 g, 1 mol), and dry acetonitrile (500 ml) are mixed in a 1000-ml round-bottom flask with a reflux condenser (potassium hydroxide drying tube) and heated under reflux for 24 h. After cooling, the acetonitrile is removed and the residue treated with isopropyl alcohol (200 ml). Ether is then added until the solution retains a very slight turbidity and then seeded or rubbed. After crystallization is complete the precipitate is filtered off under suction, washed

with ether, and the ether-moist product dried in a water-pump vacuum. The product is hygroscopic. Yield 192.2 g (76%), m.p. 85.0–86.5 °C.

2,5-Undecanedione[5]

Heptanal (57.1 g, 0.5 mol), butenone (35.1 g, 0.5 mol), and Cat. 1 (13.5 g, 0.05 mol) are united in a 250-ml three-necked flask fitted with stirrer, reflux condenser (with drying tube), dropping funnel, and gas entry tube. Triethylamine (30.3 g, 0.3 mol) is rapidly added from the dropping funnel; the mixture is stirred with heating under nitrogen for 8 h. Work-up is by pouring into 1% sulfuric acid (500 ml), thorough shaking, and extraction with chloroform (4 × 100 ml). The chloroform phase is washed with water, sodium hydrogen carbonate solution, and once again with water. After removal of chloroform the mixture is distilled over a 30-cm Vigreux column. Yield 71.8 g (78%), b.p. 128 °C/8 torr, m.p. 33–34 °C (from pentane, −18 °C).

If the reaction is performed in ethanol (500 ml) with the same quantities of starting materials then 12 hours' refluxing are required. After removal of the ethanol by distillation, the mixture is worked up in the same way; yield *ca.* 72%.

1-Phenyl-1,4-pentanedione[15]

A solution of freshly distilled benzaldehyde (10.6 g, 100 mmol) and anhydrous DMF (50 ml) is added dropwise within 10 min to a stirred mixture of sodium cyanide (0.49 g, 10 mmol) and DMF (50 ml) at 35 °C. After 5 minutes' stirring, a solution of freshly distilled methyl vinyl ketone (5.3 g, 75 mmol) in DMF (100 ml) is added at 35 °C over 20 min. Stirring is continued for 1 h at the same temperature and the reaction mixture then treated with twice the amount of water. After repeated extraction with chloroform the combined extracts are washed with dilute hydrochloric acid (pH 2), then with sodium hydrogen carbonate solution, and finally with water. After removal of solvent, the residue is vacuum distilled. Yield 10.8 g (82%), b.p. 93–94 °C/0.1 torr, m.p. 28–29 °C (from isopropyl alcohol).

2,4-Di(2-furyl)-1-phenyl-1,4-butanedione[9]

Benzaldehyde (6.9 g, 0.06 mol), 1,3-di(2-furyl)-2-propen-1-one (9.3 g, 0.05 mol), Cat. 2 (2.5 g, 0.01 mol), triethylamine (10.1 g, 0.1 mol), and dry ethanol (25 ml) are united in a 100-ml three-necked flask fitted with a stirrer, a gas tube, and a reflux condenser with a potassium hydroxide drying tube. The mixture is stirred for 15 h at 70 °C in a slow stream of nitrogen. After cooling the volatile components are distilled off in a water-pump vacuum. The residue is taken in water (200 ml) and dilute H_2SO_4 (25 ml), thoroughly shaken, and extracted several times with $CHCl_3$. The combined organic phases are washed with sodium hydrogen carbonate solution and a little water and then dried with $MgSO_4$. After filtration the solvent is distilled off and the residue recrystallized from isopropyl alcohol. Yield 12.0 g (82%), m.p. 79–80 °C.

1-Oxo-2-(2-oxopentyl)tetralin[19]

2-(Dimethylaminomethyl)-1-oxotetralin (40.4 g, 0.2 mol), Cat. 1 (10.78 g, 0.04 mol), and anhydrous DMF (200 ml) are transferred into 500-ml three-necked flask fitted with a stirrer, reflux condenser with drying tube (KOH), and a pressure-equalizing dropping funnel with nitrogen entry tube. After warming to 80–90 °C, triethylamine (16.2 g, 0.16 mol) is added; butyraldehyde (28.84 g, 0.4 mol) is subsequently added dropwise over 1.5 h. The reaction mixture is stirred for another 2 h. The solvent is then distilled off and the oily residue added to water (500 ml). The aqueous phase is acidified with dilute hydrochloric acid and extracted with ether (4 × 100 ml). The combined ether extracts are neutralized with dilute $NaHCO_3$ solution, washed with water, and then dried over Na_2SO_4. Removal of ether is followed by vacuum distillation of the residue. Yield 32.8 g (72%), b.p. 134 °C/0.2 torr.

1,4-Di(2-thienyl)-1,4-butanedione[17]

A solution of freshly distilled 2-thiophenecarbaldehyde (14 g, 125 mmol) in anhydrous DMF (40 ml) is added to a mixture of sodium cyanide (10 mmol) and DMF (40 ml). After addition of 3-dimethylamino-1-(2-thienyl)-1-propanone (18.3 g, 100 mmol; from 22.5 g of hydrochloride) in DMF (100 ml), stirring is continued for another 2 h prior to addition of twice the amount of water. After repeated extraction with chloroform the combined extracts are washed neutral. The solvent is distilled off and the residue recrystallized from ethanol. Yield 18.8 g (75%), m.p. 130–131 °C.

5,8,11-Pentadecanetrione[20]

Cat. 1 (7 g, 0.025 mol), triethylamine (30 g, 0.3 mol), divinyl ketone (11 g, 0.135 mol), and pentanal (26.4 g, 0.30) are successively introduced into a 250-ml three-necked flask fitted with a reflux condenser carrying a KOH drying tube, a stirrer, and a gas inlet tube. The mixture is heated under nitrogen up to an oil-bath temperature of 65 °C. After distilling off the triethylamine, the residue is dissolved in chloroform and the chloroform phase washed with sodium hydrogen carbonate and common salt solution. The aqueous phase is again extracted with chloroform and the combined chloroform phases concentrated *in vacuo*. The residue is recrystallized from methanol. Yield 20.5 g (62%), m.p. 84 °C.

4-Oxo-4-phenylbutyronitrile[24]

A solution of freshly distilled benzaldehyde (10.6 g, 0.1 mol) in anhydrous dimethylformamide (50 ml) is added over 10 min to a stirred mixture of sodium cyanide (2.45 g, 0.05 mol) and dimethylformamide (50 ml) at 35 °C. Stirring is continued for another 5 min and then freshly distilled acrylonitrile (4.0 g, 0.075 mol) in dimethylformamide (100 ml) is added dropwise over 20 min at 35 °C. The mixture is stirred for 3 h at the same temperature and then treated with twice the amount of water. After repeated extraction with chloroform the combined extracts are washed with dilute sulfuric acid (pH 2), then with sodium hydrogen carbonate solution, and finally with water. The solvent is removed and the residue vacuum distilled. Yield 9.5 g (80%), b.p. 114 °C/0.3 torr, m.p. 70 °C.

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Molecular Complexes and Oxygen Adducts of Tetrapyrrole Pigments

By Jürgen-Hinrich Fuhrhop[*]

Metalloporphyrins not carrying functional groups and the π-radicals of these species form comparably stable coplanar π-π-dimers by means of various types of weak interactions. Chlorophyll a and other derivatives containing carbonyl groups add water and aggregate into molecular complexes by means of hydrogen bonds. Such aggregates are of special interest in connection with a new hypothesis for the photo-oxidation of water to oxygen during photosynthesis. Finally, some new discoveries concerning the structure and reactivity of heme-oxygen complexes are discussed.

"I think that a great field which we can call chemistry or can call molecular biology, if we want, in which there are possibilities of tremendous progress, is the field of the explanation of the highly specific weak interactions between molecules showing up in biological systems.

I think that the various phenomena of biological specificity are determined by the rather weak interactions between molecules ... the sitting together of two molecules over a considerable area so that the forces of attraction are summed up over this area into an effective bond between the molecules. Here we are pretty largely ignorant still. We don't know why it is for the most part ..., why one drug is physiologically active and another substance is not physiologically active. We may have some rather vague general ideas about why this takes place, but these need to be made specific. We need to get a penetrating and reliable theory of the weak interactions between molecules responsible for biological specificity and in general of the dependence of the physiological properties of substances on their molecular structure.

I consider this a branch of chemistry and I think that this is a field in which there should be tremendous progress during the next decade or two".

Extract from an interview with Prof. Linus Pauling (Men and Molecules, the unique ACS radio series No. 366, "The Committed Scientist", around 1970).

1. Introduction

Linus Pauling's answer to the question on further development of chemistry opens up the chapter of modern natural product chemistry of greatest interest to the author of this review. Not only the determination and synthesis of primary structures appear to him to deserve the closest attention, but also the discovery of the specific interactions between biologically active materials. For the organic chemist this means, first of all, the preparation and analysis of simple molecule complexes and an attempt to understand the fundamental noncovalent bonding forces. For such work associations of symmetrical molecules are initially preferable, since their spectra, crystal structure, and reaction patterns are naturally easier to interpret than those of structurally very complex components. Among the associations the simplest to analyze are generally the dimers, since their properties can be correlated directly with one monomeric molecule. Dimers of a natural product, often with solvent molecules as integrating components, are therefore usually the first object of study. Once the noncovalent reactivity of a class of compounds has been more or less clarified, complexes with other types of natural products can be analyzed, and here the choice of mixed associations will be greatly influenced by biochemical findings. The present review describes the properties of some important molecular complexes of porphyrins, chlorophylls, and bile pigments, as well as those of their derivatives. At the same time, when it appears useful, the relationships to observations and models used by the biochemist and biophysicist will be indicated.

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2. Dimers and Higher Aggregates of Porphyrins not Possessing Functional Side Chains

Porphyrins and their metal complexes behave in solution similarly to the polycyclic arenes: they form sandwich dimers with an interplanar separation of 3.5—4 Å (Fig. 1a). The bonding relationships in such dimers have been briefly discussed for the ground state by *Chandra* and *Sudhindra* for the cases of naphthalene and anthracene[1]. The following were considered to be the important components of the bonding forces in dimers:

a) *Electrostatic interactions* between the σ-electron charges on the ring carbons (*ca.* −0.1) and the positive partial charges on the hydrogens (*ca.* +0.1) of the neighboring molecule;

b) *Delocalization of the π-electrons* over both molecules:

c) *π-π-Dispersion forces, i.e.* forces of attraction between the π-electrons of one molecule and the atomic nuclei of the other. *Coulson* has shown that, in comparison with these, in molecules containing more than four double bonds the σ-σ-dispersion forces are negligibly small[2] (van der Waals-London forces).

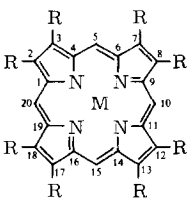
The bonding interactions are opposed by two types of repulsion forces: those between π-electrons and those between positivized hydrogen atoms or substituents in neighboring molecules. The bonding enthalpies of naphthalene and anthracene dimers amount to about 3 kcal/mol; for porphyrin dimers appreciably larger values have been measured (6 to 10 kcal/mol)[3], presumably due simply to the larger molecular surfaces, which lead to larger van der Waals-London forces.

d) *Hydrophobic or, more generally, "solvophobic" effects* play an important part, presumably because of the large surface of the porphyrins. Effects of this kind in aqueous media have often been investigated[4]. If apolar molecules are suspended

in an aqueous medium, the hydrogen bonds of the water are broken without their place being taken by other polar interactions. To reduce to a minimum this energetically unfavorable boring of holes through the water structure, the hydrophobic agents are compressed to molecular aggregates, to oil droplets. It may be assumed that the aggregation of porphyrins is favored by analogous disturbances in the solvent structure of polar organic solvents[5] such as methanol and acetonitrile.

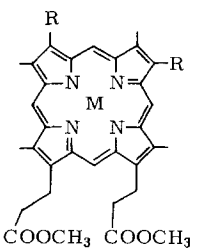
e) *π-Radicals of the chromophore* can bunch together to diamagnetic dimers, whereby there is formed either a new σ-bond in the molecular plane (*e.g.* the dimer of the triphenylmethyl radical, $\Delta H = -11.5$ kcal/mol)[6, 7] or a π-π-bond perpendicular to the molecular plane (*e.g.* the dimer of the *N*-ethyldihydrophenazinyl radical, $\Delta H \approx -2$ kcal/mol)[8].

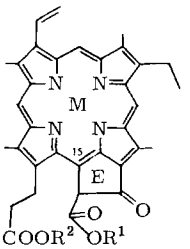
None of the above five types of bonding forces can be measured directly. Our knowledge is limited to the total bonding enthalpies and structures of the dimers, from the changes in which on variation of chromophore, substituents, and the medium one can draw qualitative conclusions about the nature of the bonding forces.



(1a), R = H, M = 2 H
(1b), R = CH_3, M = 2 H
(1c), R = C_2H_5, M = 2 H
(1d), R = H, M = Mg
(1e), R = H, M = Zn
(1f), R = C_2H_5, M = Mg
(1g), R = C_2H_5, M = Zn
(1h), R = C_2H_5, M = Cu
(1i), R = C_2H_5, M = VO

Porphine *(1a)*, the unsubstituted parent compound of the porphyrins, is sparingly soluble in organic solvents and exists in the form of ill-defined aggregates. This is expressed, for example, in complicated, strongly solvent-dependent, and often time-dependent electronic spectra with broad shoulders on the absorption bands. Octamethylporphyrin *(1b)* is still more strongly aggregated and almost insoluble in all solvents, presumably because of its greater molecular weight, the higher electron density in the chromophore, and the greater number of hydrogen atoms. Octaethylporphyrin *(1c)*, however, and all higher homologs are more soluble by one to two orders of magnitude than porphine in chloroform, pyridine, *etc.* Similarly, all the hydrophobic derivatives of the natural porphyrins and chlorophylls, *e.g.* protoporphyrin dimethyl ester *(2a)*





(2a), R = $CH{=}CH_2$, M = 2 H
(2b), R = C_2H_5, M = Co^{II}
(2c), R = $CH{=}CH_2$, M = Fe^{II}

(3a), $R^1 = R^2 = CH_3$, M = 2 H
(3b), $R^1 = CH_3$, R^2 = Phytyl, M = Mg
(3c), $R^1 = R^2 = CH_3$, M = Mg
(3d), $R^1 = R^2 = C_2H_5$, M = Mg

and methylpheophorbide a *(3a)*, are very readily soluble in many organic solvents[9]. These surprising and by no means trivial solubility differences are probably caused by space filling by the alkyl side chains, which prevent aggregation beyond the dimer stage (Fig. 1). The crystal structures of nearly all porphyrins studied so far—here, however, including porphine[10, 11]—contain porphyrin dimers as repeat units (separation of porphyrin planes 3.4 to 4.2 Å).

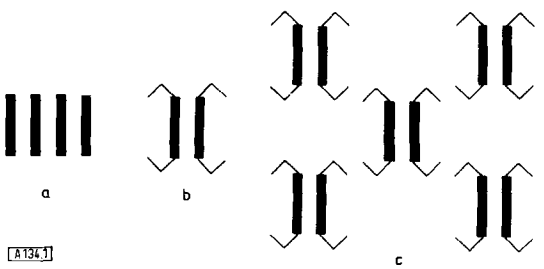


Fig. 1. a) Unsubstituted planar compounds showing large flat areas, which include *e.g.*, unsubstituted porphine *(1a)*, and form dimers or higher aggregates in which the molecular planes lie one over the other with a separation of 3.5 to 4.5 Å. b) Porphyrins with several fairly large substituents, *e.g.* ethyl groups, still form dimers but further aggregation is difficult. Radicals from porphyrins and chlorophyll, for example, afford diamagnetic dimers in completely reversible reactions but do not form insoluble polymers. c) The tendency to form dimers and space-filling by the substituents account for the commonest crystal structure (here shown only two-dimensionally) of porphyrins and their metal complexes.

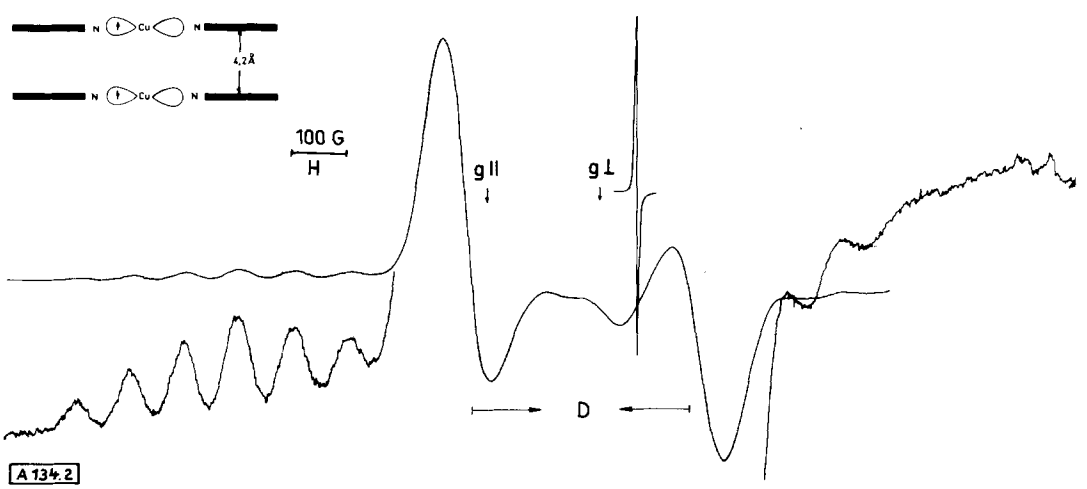


Fig. 2. When the dimer of a porphyrin radical contains copper(II) ions, *e.g. (1h)*, a molecule in the triplet state results, since the two unpaired copper electrons are localized largely in the porphyrin plane and cannot pair.

Electrochemical oxidation of the magnesium *(1d)* or zinc *(1e)* complex of porphine to the π-radical cation leads to formation on the platinum electrode of a black precipitate which is insoluble in all solvents including concentrated sulfuric acid; it is presumably a graphite-like polymer of porphine[12]. π-Radical cations of the metal complexes of octaethylporphyrin *(1f)* to *(1h)*, however, do not polymerize but instead form only stable π-π'-dimers in many solvents, *e.g.* acetonitrile or methanol/chloroform (10:1). The bonding enthalpy has been measured as 14 to 18 kcal/mol, which is extremely high when compared with those of other radical dimers (see above). Moreover, a new absorption band is observed in the near infrared, with an oscillator strength of about 0.7[13]. Although no X-ray structure analysis of these diamagnetic radical dimers has yet been successful, their structure can be derived from the ESR spectra of the copper(II) complexes, *e.g. (1h)*. The unpaired electron of the copper(II) ion, which has the d^9 configuration, is localized to the extent of 98% in the $d_{x^2-y^2}$ orbital in the porphyrin plane. The ESR spectrum of the π-π'-dimer of the π-radical cation shows, as in Fig. 2, hyperfine splitting by both copper ions, and the copper-copper separation can be estimated as 4.2 Å from the coupling constants D of the signal (Fig. 2)[14]. The separation of the two copper ions, which corresponds approximately to the extension of the d-orbitals, is intelligible only if the two porphyrin planes are parallel to each other.

In the meantime we detected π-π'-dimers of porphyrin radicals from porphyrins[13], chlorins[14], and oxophlorins[15], from zinc[14], copper[14], vanadium[14], and nickel complexes, and in such different solvents as methanol[13] and toluene[14]. Bond enthalpies of 14 to 18 kcal/mol were found in all cases. From these results it can be concluded that both delocalization of π-electrons (bonding force b) and the simultaneous formation of a π-π'-bond perpendicular to the porphyrin plane by pairing of the lone electrons (bonding force e) are the determining bonding forces in these dimers. Furthermore, the bond enthalpies in polar solvents (methanol, water, acetonitrile) appear to be about 2 to 3 kcal/mol greater than in apolar solvents[13] (bonding force d).

A splendid exotic will form the last example of porphyrin dimers not containing functional groups. If a porphyrin is treated in tetrahydrofuran/dichloromethane with mercury(II) acetate, one obtains a complex containing three mercury, two acetate, and two porphyrin ions (Fig. 3), whose NMR spectrum shows weak splittings due to the interaction of the two porphyrin nuclei[16].

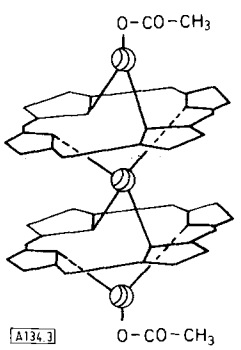


Fig. 3. Mercury(II) ions and porphyrins form together double-decker sandwich complexes that readily rearrange to normal porphyrin complexes. The structure of this dimer was derived from NMR spectra and elemental analyses.

On addition of pyridine the dimer breaks apart and the normal mercury complex is formed. This unusual association presumably owes its existence to two unusual properties of the mercury(II) ion: its relatively large ionic radius of 1.1 Å, which prevents its entry into the interior of the porphyrin, and its tendency to form covalent bonds, which makes loss of acetic acid difficult.

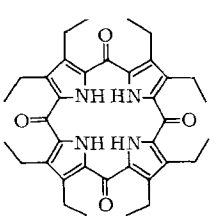
So far only the dimers of the simplest porphyrins and their metal complexes have been described above. All these are well defined and their bonding can be qualitatively well explained. However, we have already learnt about seven types of bonding, and it should be clear that bio-(in)organic chemists who plan syntheses of new molecular complexes will be faced with manifold problems[17]. The next stage of complexity is reached with porphyrin derivatives that contain carbonyl groups.

3. Dimers and Higher Aggregations of Porphyrin Derivatives Containing Carbonyl Groups

Aldehyde or ketone groups conjugated with pyrrole or porphyrin rings act as strong electron donors[18] and form hydrogen bridges with OH and NH proton donors. The strength of the bond is the greater the more easily can the OH or NH bond be broken and the richer is the carbonyl group in electrons. In other molecules NH—O and OH—O bond lengths of *ca.* 2.7 to 3.0 Å and bond angles between 120 and 180° have been found[19]. Electrostatic interactions have most commonly been assumed as the bonding principle, *i.e.* the positive hydrogen atom is attracted by two heteroatoms and simultaneously decreases the repulsion between them. In accord with this, *Allen*[20,21] recently formulated a simple and convincing model of the hydrogen bridge in which the bond energy E_D of a series of hydrogen-bridged dimers is given by eq. (a):

$$E_D = K\mu_{A-H}\Delta I/R \qquad \text{(a)}$$

where K is a constant, μ_{A-H} is the dipole moment of the monomer providing the proton, ΔI is an expression containing the difference between the ionization potentials of the two atoms bound by the proton, and R is the separation between these atoms.



• 2 H_2O *(4)*

Octaethyl-5,10,15,20-tetraoxoporphyrinogen (octaethylxanthoporphyrinogen) *(4)* forms the simplest known hydrogen-bonded aggregate of a porphyrin on which the important structure-controlling factors of this weak interaction can be demonstrated[23,24]. The molecule contains four acidic NH protons, which bind two water molecules, one above and one below the center of the porphyrinogen[25]. The requirements that the hydrogen bonds should be as nearly linear as possible, and that the van der Waals radii of the atoms concerned permit the porphyrinogens and the oxygen atoms

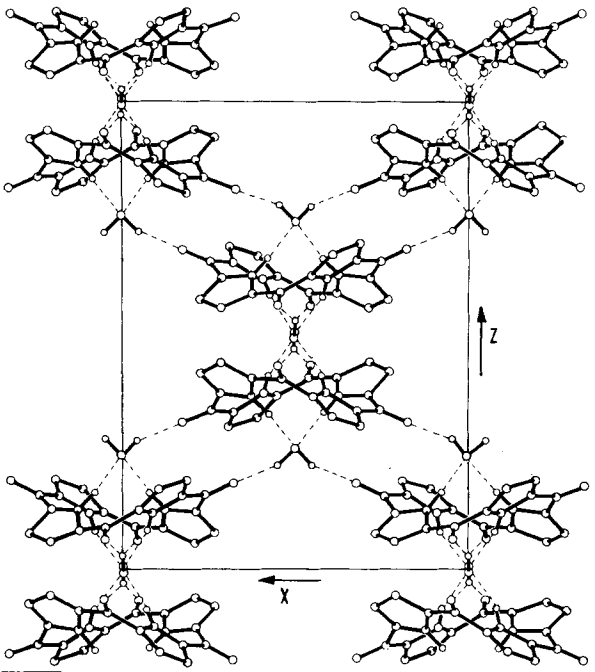
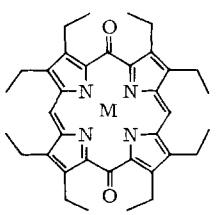


Fig. 4. Water is bonded by linear NH—O bridges above and below the center of the xanthoporphyrinogen *(4)*, leading to a wavy molecular structure. The protons of the water molecule form hydrogen bridges with the carbonyl groups of neighboring porphyrinogen molecules. The crystal lattice resembles long tubes stacked on one another, within which water molecules are fixed. The structure exemplifies an economical principle that is repeatedly observed in the molecular complexes discussed here, namely that all the acidic protons and all the oxygens are, whenever possible, linked by hydrogen bridges.

of the water to approach each other to no closer than about 2.7 Å, result in rotation of the pyrrole rings out of the porphyrin plane (Fig. 4). The dihydrate also contains the four acidic protons of the water molecules; these bind four carbonyl oxygen atoms of neighboring porphyrinogen molecules in a symmetrical manner, and this leads to cylindrical linking of the chromophore chains. The whole structure thus resembles a stack of interconnected tubes in which the positions of the water molecules are fixed with well-defined separations of 2.4 and 4.8 Å. The effect that the water has on the crystal formation of *(4)* can also be easily demonstrated macroscopically: the water of crystallization can be removed only above 150°C under high vacuum, and the crystals then disintegrate into a powder.



(5a), M = 2 H
(5b), M = Zn

Reduction of xanthoporphyrinogens by sodium tetrahydridoborate leads to the formation of 5,15-porphinoquinones such as *(5a)*, which have recently become a center of interest[15, 22, 26–28]. On chromatography of the zinc derivative *(5b)* on silica gel a stable dimer can be isolated, whose peculiar chemical reactivity (see Section 6) can be understood only when the crystal structure is recognized: each central zinc ion is bound to a molecule of methanol whose proton is hydrogen-bonded to the neighboring carbonyl oxygen; the zinc-bound methanol of the second porphinoquinone is attached to the first molecule in a similar manner, so that a dimer is formed in which the parallel porphyrin planes are shifted with respect to each other by half the length of the molecule (Fig. 5).

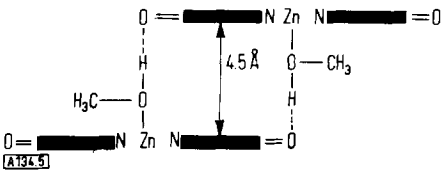


Fig. 5. Two 5,15-dioxoporphodimethene ("porphinoquinone") molecules are linked by methanol molecules bonded on the one hand coordinately to the central zinc ion and on the other by hydrogen bridges to a carbonyl group of a neighboring molecule. Semiquinone radicals formed on reduction are probably stabilized by this dimer formation.

Similar but much more complicated relationships are found in the case of chlorophyll *(3b)*. Here the central magnesium ion binds one water molecule, which can be attached to the carbonyl group of the carbocyclic ring E. Moreover, the magnesium ion itself is probably sufficiently electrophilic to add to the β-oxo ester group of ring E of a second chlorophyll molecule. These basic possibilities of association lead to a large number of dimeric and polymeric aggregates which have been clarified by very thorough NMR and IR investigations, mainly by *J. J. Katz et al.* In the present review only the two most important dimer structures elucidated by *Katz* and an X-ray structure analysis by *Strouse* will be discussed; details of the methods used in these investigations will be found in reviews by *Katz*[29–31] and in some other papers[32–34].

The principles of spectroscopic analysis of chlorophyll aggregates are based mainly on the following facts:

1. The IR absorption of the oxo group in the carboxylic ring E lies at 1695 cm^{-1}. If chlorophyll aggregates in extremely dry apolar solvents (*e.g.* CCl_4), the intensity of this band diminishes and an "association band" appears at 1652 cm^{-1}. The origin of this band can be seen in the formation of a C=O—Mg group, as indicated in Fig. 6.

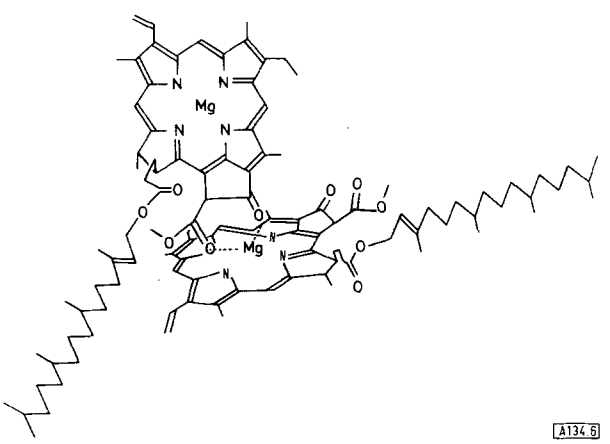


Fig. 6. In the anhydrous dimer of chlorophyll the central magnesium ion of one molecule is bound coordinately to the carbonyl groups of the carbocyclic ring E of the other molecule. The structure is based on IR and NMR data.

2. In a dimer according to Fig. 6 some parts of the two chromophores lie very close to one another, while others are further apart. Since strong ring currents are induced in

macrocycles of the porphyrin type in the NMR experiment, conclusions can be drawn about the structure of the aggregates from changes in the chemical shifts, *e.g.* of proton signals of the substituents, on increasing the concentration: the larger the shift, the closer are the two macrocycles in the region concerned. Addition of a disintegrating solvent at relatively high concentration is often used as a test: the chemical shifts must then return to values corresponding to the monomer. Analogous ^{13}C-NMR measurements lead to similar results[35].

3. In hydrated chlorophyll aggregates the band at 1652 cm^{-1} is replaced by absorption at 1638 cm^{-1}, which is assigned to a C=O...HO(H)—Mg grouping: a water molecule is inserted between the magnesium ion and the carbocyclic ring E of the neighboring molecule, and a dimer having the structure shown in Fig. 7 is obtained. This too is supported by extensive NMR data.

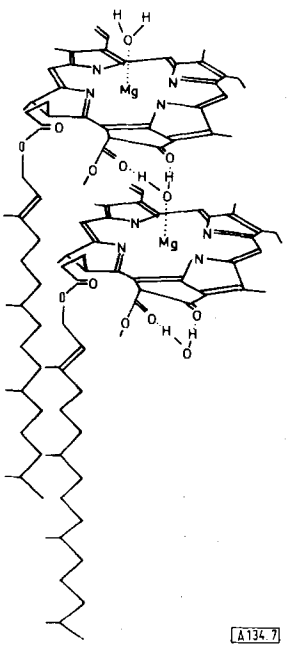


Fig. 7. If a water molecule is added to the anhydrous chlorophyll dimer (Fig. 6) a new dimer is formed, containing defined hydrogen bonds. The structure follows from IR and NMR data.

Under many different conditions the dimers can be converted into higher aggregates, whereupon shifts of the 660 nm chlorophyll absorption to 740 nm are observed in the electronic spectra. The structures of the aggregates are in many cases proved by use of deuterated derivatives, other metal complexes, or metal-free bases, by molecular-weight determinations, elemental analyses, *etc.* However, we think that complete certainty about such complex structures as those in Figs. 6 and 7 cannot be provided by NMR, ESR, or IR experiments, no matter how careful they are. Only X-ray structure analysis provides a trustworthy guide to such formations. If, on the other hand, the structure of the molecular aggregates in the crystal is in accord with all spectroscopic structural parameters obtained for a solution, then it appears permissible at the present time to conclude that the environmental relationships of at least two molecules are identical in solution and in the crystal.

Some years ago, in fact, *Strouse* succeeded in clarifying the structure of a dihydrate of ethylchlorophyllide a *(3d)* by X-ray analysis[36]. The important structural features are given in Fig. 8. One water molecule occupies the fifth coordination position of the magnesium. A second water molecule is joined to the first and to the carbonyl oxygen of the ester group on ring E by means of two hydrogen bridges. In this

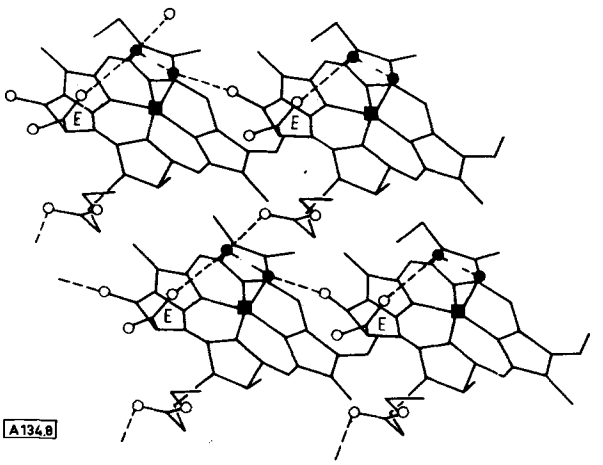


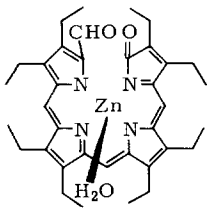
Fig. 8. X-ray molecular structure of ethylchlorophyllide a *(3d)*. Two molecules of water link the magnesium ion intramolecularly to its own carbocyclic ring E and intermolecularly to two further molecules. The resulting network structure probably corresponds in general to the structure of the light-gathering chlorophyll aggregate *in vivo*. ○ = >CO; ● = H_2O; ■ = Mg.

way one proton of each water molecule remains free for intermolecular bridging. The proton of the water bound to magnesium binds the ketone oxygen atom of ring E of a neighboring molecule, in complete agreement with *Katz*'s dimer shown in Fig. 7. A chlorophyll chain is thus formed (shown horizontal in Fig. 8). The intramolecular unbound proton of the second water molecule is linked to the carbonyl oxygen of the ester group on ring E of another molecule, whereby a second chlorophyll chain arises (that show vertical in Fig. 8). This structure provides no contradiction of importance to the structures proposed by *Katz*, but supplements them in important points about which the spectroscopic data convey no information. The reason for this is clear: superposed porphyrin macrocycles can be recognized at once in the NMR spectra, but porphyrin molecules lying side by side can barely be distinguished from monomers.

Before leaving the field of tetrapyrrole chromophores held together by hydrogen bonds, we can compare the simple crystal structure of xanthoporphyrinogen dihydrate [*(4)*] (Fig. 4) with the complicated structure of chlorophyllide a dihydrate [*(3d)*·2H_2O] (Fig. 8). In the former the two water molecules, one above and one below the plane of the chromophore, together with the bridge bonds stabilize a structure corresponding to bundles of tubes within which water molecules are fixed. In the magnesium complex *(3d)* the two water molecules lie on the same side of the chlorophyll derivative and by analogous interactions form a network on whose surface the water is coordinated. In both cases the structures can be derived directly from the properties of the components [essentially the acidity of the NH protons in *(4)*, the favored fivefold coordination of the magnesium in *(3d)*, and the electronegative carbonyl groups in *(4)* and *(3d)*]. The fundamental principles are clearly a) neutralization of positive (on the central metal) and negative (on the carbonyl groups) partial charges by attachment of water and b) coordinative saturation of all the protons capable of hydrogen bonding.

4. An Open-Chain Dimer

Photo-oxidation of metalloporphyrins with molecular oxygen leads to formylbiliverdins[37,38] *e.g.* the zinc complex *(6)*, *i.e.* it leads to fission of the macrocycle at a methine bridge. In this way conformational changes become possible that appear to be excluded for the rigid porphyrin ligands. If *(6)* is crystallized from neutral solvents, brown plates are obtained (λ_{max} = 830 nm) whose X-ray structure analysis displays a cyclic-planar ligand (Fig. 9)[39]. The same conformation in solution was proved by ESR spectroscopy for the copper complex of that ligand[40].



(6)

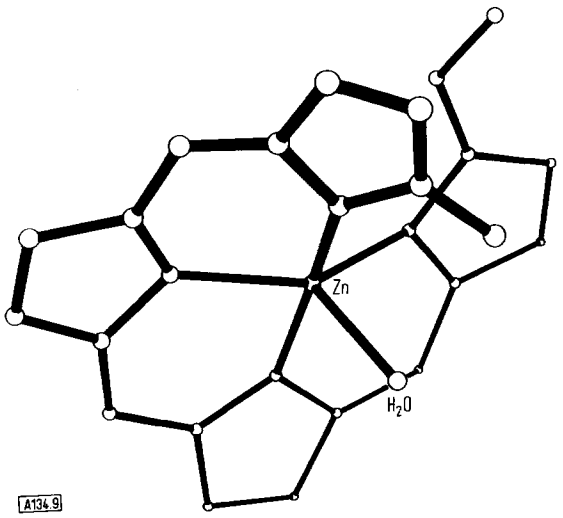


Fig. 9. Molecular structure of the zinc complex of synthetic octaethylformylbiliverdin *(6)*. One water molecule is bonded coordinately and presumably stabilizes the planar arrangement of the four nitrogens of the biliverdin ligands.

One structural peculiarity was striking, namely that the central zinc ion in *(6)* binds a water molecule. If the solution of *(6)* is acidified a reversible color change from brown to green (λ_{max} = 730 nm) is observed. Structure analysis of the green crystals disclosed a bis-helical dimer in which the two zinc ions were each bonded to one-half of both chromophores (Fig. 10). For this rearrangement the driving force is once more easy to identify, and once more a new effect comes into play: it is assumed that as the pH decreases the water molecule of the hydrate shown in Fig. 9 is protonated and immediately thereafter splits from the zinc ion.

Whereas the square-planar arrangement of ligands of the biliverdin chromophore around the zinc ion is stable in the case of the fivefold coordinated metal, after dehydration the now fourfold coordinated zinc seeks to attain a tetrahedral configuration of the four surrounding nitrogens. This is in no way possible with *one* bilatriene chromophore. Instead, two formylbiliverdin molecules intertwine so that each of the two pyrromethene units of one chromophore can engage two corners of a tetrahedron. In fact both zinc ions in the structure shown in Fig. 10 attain a tetrahedral arrangement

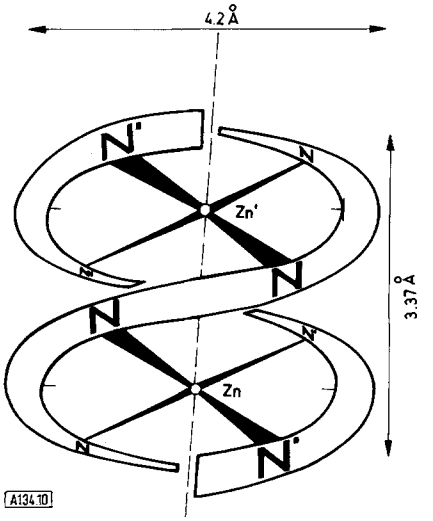
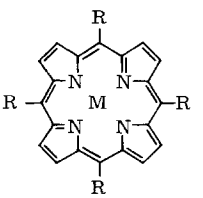


Fig. 10. If a solution of biliverdinate *(6)* is acidified, the water molecule is split off. The now fourfold-coordinated zinc ion strives toward a tetrahedral environment and attains this by reversible formation of the bis-helical dimer drawn schematically (see Ref. [39]).

of the surrounding nitrogen electrons in this way. It is now striking to find that the reaction is easily reversible: if an acid solution of the bis-helical dimer is neutralized, the structure shown in Fig. 9 is regenerated.

5. Dissociation of Aggregated Porphyrins

Hemes and chlorophylls aggregate both in aqueous solution and in an apolar medium. If the porphyrin units isolated from natural systems are required, the chromophore is fixed in a polymeric matrix. Stable iron(II)-oxygen complexes, for example, can be formed only if reaction with a further molecule is prevented (see below). For chemical and physical investigations of monomeric metalloporphyrins the synthetic porphyrins *(7a)* to *(7c)* are particularly suitable, built into micelles rather in the manner shown in Fig. 11. Proof of the resolution of *(7a)* and *(7b)* into monomers in the micelles was provided by ESR spectroscopy for the paramagnetic copper complexes *(7d)* and *(7e)*: if these copper complexes were dissolved in water an unresolved ESR spectrum was observed, whereas on addition of the micelle-forming lauryl sulfate the hyperfine structure of the monomeric copper complexes appeared[41].



(7a), M = 2 H, R = $(CH_2)_8$–COOH
(7b), M = 2 H, R = $(CH_2)_8$–CH=CH–SO_3H
(7c), M = 2 H, R = $(CH_2)_9$–$\overset{\oplus}{N}(C_2H_5)_2CH_3$
(7d), M = Cu, R = $(CH_2)_8$–COOH
(7e), M = Cu, R = $(CH_2)_8$–CH=CH–SO_3H

Hemoglobin contains four heme molecules, each of which consists of one iron(II)-porphyrin and is rigidly coordinated to one imidazole base of the globin. The average separation of the porphyrin ligands is about 30 Å (Fig. 12)[42,43]. Nevertheless, there is a very close relationship between all four chromophores; if the sixth coordination site of one heme is loaded with oxygen, then all four subunits of the hemoglobin rearrange so as to make easier similar loading of the other heme units. This phenomenon was the starting point of the *Jacob* and

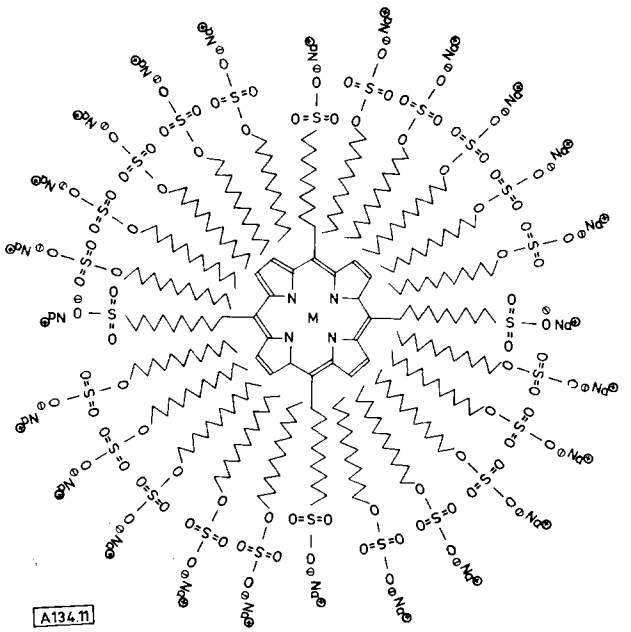


Fig. 11. By a suitable choice of detergents and substituted porphyrins, monomolecular porphyrin solutions are obtained in which the chromophore is localized in the hydrophobic interior of the micelles.

Monod allosteric model of enzyme regulation and is still today a central theme in structural chemistry.

It is now known from X-ray structure analyses of deoxyhemoglobin and of (partially decomposed) oxyhemoglobin that in the total course of oxygenation the essentially hydrophobic contact positions of the subunits change along the full lines in Fig. 12, although the overall structure of the protein remains largely unchanged. It must now be assumed that the first oxygenation leads to extensive disturbances of the interactions between the subunits, and that this accelerates the oxygenation of the other subunits[44].

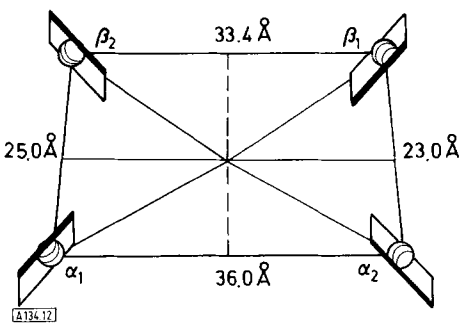


Fig. 12. The fixed relative positions of the heme molecules in oxyhemoglobin prevent their direct interaction, so that autoxidation of the heme is prevented. Nevertheless, adsorption of oxygen occurs through the four heme molecules by a cooperative action which is achieved by drastic changes in conformation on addition of the oxygen (the allosteric effect). The full lines indicate mainly hydrophobic interactions between unlike chains, while the broken line indicates the mainly polar interaction between like chains.

The structure of the unusual, water-soluble protein from *Chlorobium limicola* with a molecular weight of about 130000 and a total of twenty-one bacteriochlorophyll molecules[45] was recently clarified by X-ray spectroscopy. First it was shown that there were three identical subunits of molecular weight 42000, each containing seven bacteriochlorophyll molecules, and their structure was elucidated (Fig. 13). Here too it was assumed that the seven chromophores, each separated from the next by 12 Å, supported each other in their biological functions. The protein complex as a whole conducts excitation energy from the "antenna" chlorophyll molecules, which absorb sunlight, to the photochemical centers where the light energy is converted into chemical energy. Stepwise energy transport by the protein is obviously possible, although no direct overlapping of the chlorophyll orbitals occurs and although the space between the chlorophyll molecules consists of purely hydrophobic regions of little structure. Experimentally, fluorescence and circular dichroism measurements, which will not be discussed here, prove that all seven bacteriochlorophyll molecules of one subunit are connected with one another by exciton interactions[45]. For separations >20 Å, such as must be overcome for energy transport between the subunits, the Förster mechanism can be brought into play[45].

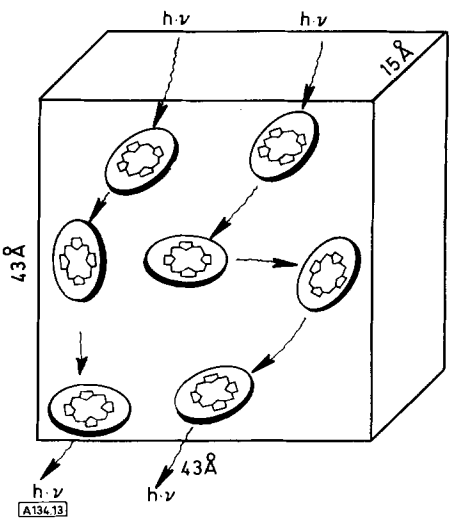


Fig. 13. The here strongly schematized molecular structure of a water-soluble bacteriochlorophyll protein shows that the chromophore molecules are not aggregated and that the space between them is strongly hydrophobic. Exciton and Förster mechanisms are discussed in relation to the transfer of quanta between the bacteriochlorophyll molecules of this light-conducting complex.

In nature all intermediate stages are found between, on the one hand, very extended aggregates resembling a crystal surface, in which the porphyrins are directly coupled to one another and, on the other, complexes in which high-molecular proteins contain isolated porphyrin islands. These complicated structures have often been characterized only by electronic spectra and lengthy biochemical interpretations. The few complexes discussed in this review form a solid nucleus for further work; they show that porphyrins usually act cooperatively and that the structure of biological, high-molecular porphyrin complexes at once also defined the mode of action: the "crystal flatness" of extended chlorophyll is suitable for collection of light, the parallel arrangements of chlorophyll chromophores with a separation of 20 Å are optimally suitable for the conduction of light, and the regulation of oxygen-absorption is best effected by flexible proteins with isolated porphyrin islands.

6. The Chemical Reactivity of Porphyrin Aggregates

Since the aggregates described in the preceding sections have been discovered and elucidated only recently, very little is known of their chemical reactivity in comparison with the monomers. Fundamental differences are to be expected above all in photo- and redox-chemistry, since in sandwich

dimers the unpaired electrons of triplet states and radicals can be smeared over the two π-systems and the axial ligands. Two examples, recently discussed but still somewhat speculative, may illustrate this point.

If the zinc complex *(5b)* is reduced by dithionite in hexamethylphosphorotriamide, then only the dimer with bridging methanol forms a semiquinone radical that is stable for hours under nitrogen, whereas the monomer decomposes irreversibly under these conditions within a few seconds. Furthermore, the ESR signal of the semiquinonoid radical is extremely narrow (<1 gauss), which indicates distribution of the unpaired electrons over two or more molecules. It seems reasonable to assume that the hydrogen bridge protons of the structure shown in Fig. 5 achieve considerable stabilization of the semiquinone radical anions formed in the reduction.

There are at present two contradictory theories about the role of chlorophyll dimers in the oxidation of water, and these enliven the interest in these aggregates.

According to *Katz*[31], a water-bridged chlorophyll dimer (Chl HOH Chl) at the photosynthesis reaction center is linked to the antennae-chlorophyll aggregate $(Chl_2)_n$ (see above) and to an electron-acceptor and an electron-donor:

	$X^{\ominus}$	
$(Chl_2)_n$	[Chl HOH Chl]	Y
antennae chlorophyll	"special pair" $X^{\ominus}$ = electron donor	electron acceptor

The assumption of a special chlorophyll dimer ("special pair") at the reaction center is supported here again by the observation of a particularly narrow ESR signal (line width *ca.* 1 gauss) for the oxidized photoreaction center, and this permits distribution of the unpaired electrons over at least two chromophore molecules to be assumed. Irradiation of this complex is held to lead, by way of the excited state, to a new charge distribution in the dimer in accordance with:

	$X^{\ominus}$	
$(Chl_2)_n$	$[Chl^{\oplus}\ OH^{\ominus}H^{\oplus}\ Chl^{\ominus}\cdot]$	Y

Thereafter the chlorophyll radical cation oxidizes first $X^{\ominus}$ and indirectly water, while the chlorophyll radical anion maintains the reductive part of the photosynthesis by way of Y.

Experimentally, both *Katz*[31] and *Dutton et al.*[46] have demonstrated the occurrence of the triplet state in photosynthesis, and this could indicate the above cation-anion radical pair.

Whereas *Katz* bases his considerations on the unsymmetrical dimer of Fig. 7, *Fong*[33,34] and *Wang*[47] assume a symmetrical sandwich dimer containing two water molecules, and make the interesting speculation that its triplet state might have an unusually long life. If this were so, the energy of a singlet state from the antennae-chlorophyll could be added to the energy of the relatively low-lying dimer-triplet state. Thus, the oxidation of water could be effected in two steps [eq. (b) and (c)], each involving one energy-rich charge-transfer triplet state $Chl^{\oplus}\cdot(H_2O)_2Chl^{\ominus}\cdot$ without the necessity to invoke further redox systems (*e.g.* the often postulated manganese ion of higher oxidation numbers).

$$H_2O \xrightarrow{h\cdot\nu} OH^{\bullet} + H^{\oplus} + e^{\ominus} \qquad (b)$$

$$OH^{\bullet} \xrightarrow{h\cdot\nu} O + H^{\oplus} + e^{\ominus} \qquad (c)$$

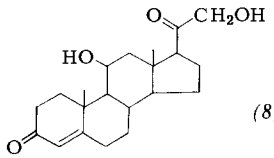
Currently attempts are being made throughout the world to synthesize porphyrin aggregates in solids in order to cleave water by sunlight in analogy to the natural process. A first, hitherto unconfirmed, success has been announced by *Wang*, who covered aluminum foil with *ca.* seventy monomolecular layers of zinc porphyrin, dipped this deeply colored photoanode into an iron(III) salt solution, and on irradiation with red light obtained potentials *ca.* 1 volt greater than that of a platinum electrode; two electrodes arranged one behind the other led to evolution of oxygen from water[47]. If this experiment and its interpretation withstand critical testing, then intensive investigations of this system with a view to industrial utilization would appear attractive. Experiments with lipid membranes are already a center of interest. If an aqueous solution of an oxidizing agent (*e.g.* Fe^{3+}) is separated by a bimolecular lipid membrane from a solution of a reducing agent (*e.g.* Fe^{2+}), the two solutions are stable next to each other for a long time: no electron transport takes place through the membrane. If, however, the membranes contain oxidizable porphyrins, *e.g.* chlorophyll, then a slow charge equalization between the two solutions can be observed, and light accelerates this by many orders of magnitude. At the same time photopotentials of about 100 mV appear between the membrane surfaces[48], these corresponding approximately to the pH-gradients that arise in photosynthesis on the membrane of vesicles of the photosynthetic system (thylacoids). Very little is yet known about the importance of porphyrin aggregation in this system.

Finally, an evolutionary-historical point may be noted. The photosyntheses that we observe today are based on the reversible formation of energy-enriched and thus chemically extremely reactive molecular states (triplet states, radicals). In monomolecular solutions, *e.g.* in chloroform, chlorophyll is decomposed very rapidly on irradiation and oxidation. In aggregates, however, the unpaired electron of the chromophore molecule is distributed over at least two partners, greatly reducing the reactivity of the individual centers in the molecule and thus protecting the system from destruction.

It is perfectly conceivable that in prebiotic time—and particularly then—organic molecules had a chance of surviving and becoming components of biological systems if, first, they could assume a useful role (here conversion of sunlight into chemical energy), and, secondly, if they did not themselves fall victim to their own functional reactivity. Other examples could be seen in the protection of nucleic and amino acids, which are sensitive to hydrolysis and redox systems, by integration into the complex structures of polymers (≈aggregates).

7. Molecular Complexes of Porphyrins with Other Natural Products

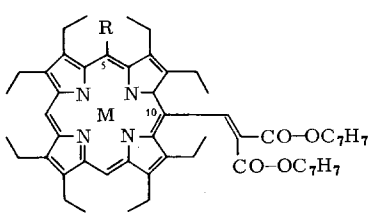
Although interest is nowadays concentrated on chlorophyll dimers in connection with the reaction center for photosynthesis, aggregates with other natural π-systems have also been studied. In particular, flavins[49] and quinones[50] form with chlorophyll charge-transfer complexes that may perhaps be involved in the redox chains of photosynthesis. So far, however, the structure is not known for any of these complexes, and we shall therefore not treat them further here. However, detailed CIDNP investigations have been reported for quinone complexes[50b].



(8)

Complexes between paramagnetic metalloporphyrins and steroids[51] are of a different type. *Hill et al.* have investigated these complexes by NMR methods similar to those used by *Katz* for chlorophyll aggregates. A 5×10^{-2} molar solution of corticosterone *(8)* showed, for example, that on titration with the cobalt(II)-porphyrin *(2b)* strong paramagnetic shifts of the protons on Cl > C2 > C3 > C4 > C11 occurred, while the other signals were hardly shifted at all. As a result of these findings and of systematic measurements of relative line widths, a 1:1 molecular complex was postulated with the following structural details. The steroid lies parallel to the porphyrin and presents its unhindered α-side to the latter; the mean separation between the two molecules is 5 to 8 Å, with C9 of the steroid lying approximately over the center of the porphyrin. The predominant bonding force between the porphyrin as a prototype of an aromatic natural product and the steroid with its rigid cycloalkene system is presumed to be electrostatic—as the bonding forces described in Section 2. In the physiologically important iron(II) complexes coordinated water could drastically alter the structure by the formation of hydrogen bonds and be the "specifying" factor. Such complexes are of extreme interest in connection with the specific oxidation of steroids by heme catalysts and molecular oxygen (see Section 9).

In this connection a remarkable observation on [2,2-bis(benzyloxycarbonyl)vinyl]porphyrins *(9a)* and *(9b)* should be noted. The phenyl group of the benzyl ester grouping lying



(9a), M = Cu, R = CHO
(9b), M = Ni, R = H

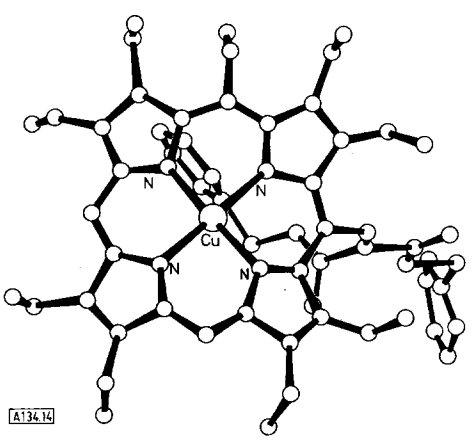


Fig. 14. Molecular structure of the dibenzyl ester of porphyrin *(9a)*. The phenyl group *cis* to the porphyrin sits *perpendicularly* almost directly above the center of the porphyrin.

cis to the porphyrin occurs in solution exactly above the center of the macrocycle; this can easily be demonstrated by NMR spectroscopy of *(9b)* and can be ascribed to interactions of the type discussed in Section 2 (types a to c). X-Ray structure analysis shows that the phenyl group in *(9a)* lies *perpendicular* to the plane of the porphyrin (Fig. 14); this was hardly to be expected in view of the current ideas on interactions between π-systems[52]. Now it has been found, in somewhat remote analogy to our case, by physical investigations of benzene, that this compound also is aggregated, and indeed always in such a way that two benzene rings are perpendicular to one another. This conformation is retained even in the gas phase[53]. The possible binding force has been only tentatively indicated (quadrupole interactions?).

8. Oxygen Complexes of Iron(II)-Porphyrins

This area has been studied unusually intensively during the last five years and shows the miserable "signal-to-noise ratio" typical of popular subjects. In other words, most of the experimental papers on oxygen complexes are repetitive in nature. In what follows we shall try to indicate the most important lines of development.

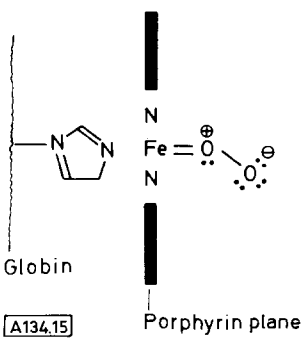


Fig. 15. The electron structure of the oxygen-bonding center in oxyhemoglobin according to *Pauling*.

Many years ago *Linus Pauling* suggested the electron structure reproduced in Fig. 15 for the oxygen adduct of the heme in hemoglobin (oxyhemoglobin, HbO_2)[54]. This structure takes account of the diamagnetism of the HbO_2, explains the increased acidity of the imidazole in HbO_2 ($pK = 6.8$) in comparison with free Hb ($pK = 7.8$), maintains the electron neutrality of the central iron atom in heme, and permits the following verifiable, specific predictions: the angle between the Fe—O and the O—O bond should be about 120°. The Fe—O bond should be as long as, or shorter than, the sum of the covalent radii (≈1.9 Å), and the oxygen atom should show IR bands and O—O bond lengths corresponding approximately to a single bond. Furthermore, the oxygen molecule should be polarized but not negatively charged in the sense of a hyperoxide anion ($Fe^{III}—O_2^{\ominus}$). Recently the first oxygen complex of "picket-fence" iron porphyrin was obtained in crystalline form—such a complex is sterically protected on one side by the fence, and a provisional X-ray structure analysis, to be accepted with caution ($R = 0.15$), has been published[55] (Fig. 16). This structure agrees beautifully with *Pauling*'s predictions[56]: the oxygen is indeed attached end-on at an angle ($\alpha_{exp} = 136°$), and the Fe—O and O—O separations amount to 1.75 and 1.24 Å, respectively. However, the IR stretching vibration of the O—O bond in the above oxygen

complex is reputedly at 1385 cm^{-1}, which has not been found for any other end-on oxygen complex; indeed, all the complexes so far characterized as of this type show a band near 1100 cm^{-1}[62], which is close to that in potassium hyperoxide KO_2 ($\nu O_2 = 1145\ cm^{-1}$). The absence of this band in the picket-fence oxygen complex leaves open some doubt about the molecular structure proposed[76].

The problem of the electronic structure of the active center in HbO_2 is, however, by no means resolved. The relative stability of the iron(II)-oxygen complex shown in Fig. 16 already provides important clues. Other iron(II)-porphyrins,

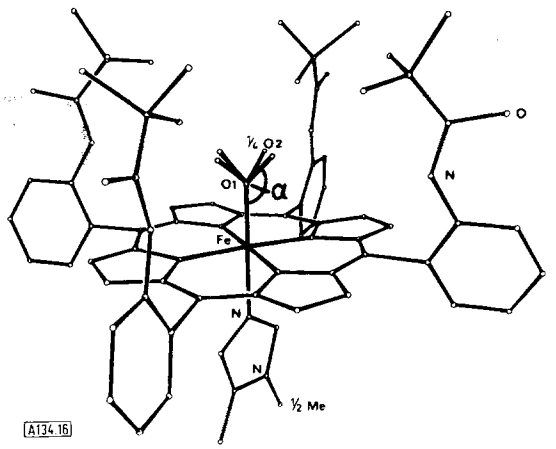


Fig. 16. Provisional and still disputed [76] molecular structure of the iron(II)-oxygen complex of the α,α,α,α-atropic isomer of *meso*-tetrakis(*o*-pivalamido)-porphyrin. This compound is the first crystalline iron-porphyrin oxygen complex. The structure corresponds to *Pauling*'s prediction.

e.g. protoheme *(2c)*[57] and tetraphenylheme[58], form analogous complexes with oxygen in the presence of imidazole derivatives below −40 °C; at higher temperatures irreversible oxidation to iron(III)-porphyrins sets in. This difference probably rests on the fact that the oxygen molecule in the complex of Fig. 16 is sterically so shielded that the addition of a second iron(II)-porphyrin and subsequent autoxidation according to eq. (d) cannot occur[59] (B = base, *e.g.* imidazole):

$$\begin{aligned} &B{-}Fe^{II}O_2 + Fe^{II}{-}B \rightleftarrows B{-}Fe^{II}O_2Fe^{II}{-}B \\ &\rightarrow 2\,B{-}Fe^{III}{-}O^{\bullet} \xrightarrow{2B-Fe^{II}} \\ &\quad 2\,B{-}Fe^{III}{-}O{-}Fe^{III}{-}B \end{aligned} \qquad (d)$$

Nevertheless, the complex shown in Fig. 16 is also oxidized rapidly in protonic solvents and more slowly in aprotic ones, giving iron(III)-porphyrins, for which the proton-catalyzed reaction (e) seems suitable:

$$Fe^{II}O_2 + H^+ + H_2O \rightarrow Fe^{III}OH + H_2O_2 \qquad (e)$$

In the above case the proton could be derived from the amide groups with which the porphyrin is substituted.

Finally, *Caughey* showed that the oxygen in oxyhemoglobin can be split off by anions (*e.g.* Cl^-, N_3^-)[60] or by reducing agents (*e.g.* hydroquinone, salicylic acid)[61], affording hyperoxide anion, while the iron is oxidized to the trivalent state [see, *e.g.* eq. (f) and (g)].

$$HbO_2 + ArO^- \rightarrow HbO_2^- + ArO^{\bullet} \qquad (f)$$

$$HbO_2^- + 2H_2O \rightarrow HbOH + H_2O_2 + OH^- \qquad (g)$$

The resistance of oxyhemoglobin to autoxidation thus apparently rests not on a special type of bonding of the oxygen but rather on shielding of the bonding center against reducing agents (including a second iron(II)-porphyrin) and nucleophiles.

In *Hill*'s hands[63] an important experiment has confirmed, in particular, *Pauling*'s and *Caughey*'s picture of oxyhemoglobin. *Hill* treated an iron(III)-porphyrin at low temperatures (to prevent dimerization) with electrochemically produced hyperoxide anions and obtained an oxygen complex whose spectrum corresponded to a large extent with that of oxymyoglobin. It should also be pointed out that there is a paramagnetic analog of the diamagnetic HbO_2: If the iron-porphyrin is replaced by a cobalt-porphyrin, then that too adds oxygen; in this case the oxygen molecule clearly exists as a hyperoxide anion and can be identified by ESR spectroscopy[64, 65].

Summarizing, it can be stated that kinetic stabilization of an iron-oxygen complex in the porphyrin series should succeed when dimerization of two heme molecules can be prevented in a hydrophobic, proton-free environment; this concept is realized in the biological heme enzymes in which the porphyrin is bound covalently or coordinatively in a hydrophobic matrix (see for example Fig. 15). More recent experiments have shown that free iron(II)-porphyrins or their oxygen complex can be kept unchanged for as long as desired in synthetic hydrophobic polymers[66, 67]; there, however, it is presumably the inflexibility of the synthetic polymers that makes the addition of oxygen slower by many orders of magnitude than it is in HbO_2.

The occurrence and strength of the end-on bond of the oxygen to heme depend largely on the π-donor-acceptor properties of the axial ligands in *trans*-positions. Oxygen complexes are stabilized considerably better by imidazole than by *e.g.* piperidine or pyridine[68]. If axial ligands are completely absent, then 1:1 oxygen complexes with heme are formed only in the crystalline state and their ESR spectra demonstrate the occurrence of a high-spin iron(III)-porphyrin radical anion [($g = 6$) and ($g = 2$) signals]. The IR spectrum shows a stretching vibration band at 1600 cm^{-1} that is very similar to the band of the free oxygen molecule ($\nu_{O_2} = 1555\ cm^{-1}$), and the visible electronic spectrum also indicates the occurrence of a π-radical.

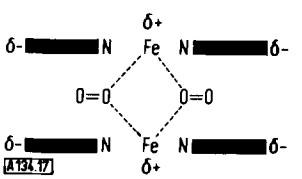
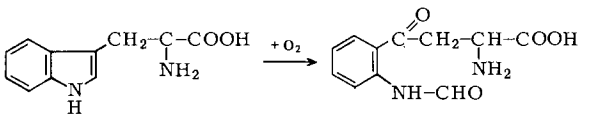


Fig. 17. Iron(II)-porphyrins without axial ligands form, with oxygen, molecular complexes in which the central iron ion probably transfers electrons to the oxygen, and this oxygen then undergoes back-bonding to the porphyrin ligands. Indications of this structure are obtained mainly from IR and ESR spectra.

If the oxygen is pumped off, the iron(II)-porphyrin is regenerated. Thus, the structure is revealed as probably a dimeric heme in which two oxygen molecules are bonded by weak donor-acceptor interactions to the positive charge centers of the two iron(III) ions and to the negatively charged porphyrin radicals.

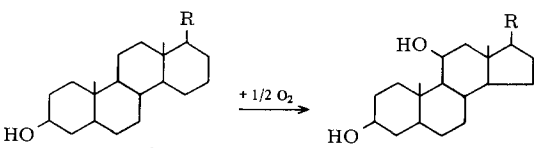
9. Reactivity of the Heme-bound Oxygen *in vivo* and *in vitro*

Ascorbic acid, phenoxide ions, and other easily oxidized substrates are rapidly oxidized even by the oxygen of oxyhemoglobin (HbO_2)[61]. Tryptophan-oxidase is a heme enzyme that, similarly to hemoglobin, is built of four subunits and catalyzes the addition of an oxygen atom to tryptophan *(10)*.



(10)

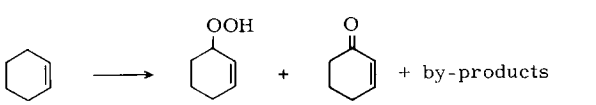
The "hyperoxide anion" of HbO_2 is here presumably bonded also to a copper ion, which could explain the special reactivity of the oxygen[69]. The most reactive and thus the most interesting heme enzyme is cytochrome P 450, which introduces oxygen atoms into unactivated CH_2 groups, formally as in *(11)*.



(11)

Cytochrome P 450 acts as the end of a short electron-transport chain that does not form ATP, and with oxygen it probably forms an extremely electron-rich iron(II)-hyperoxide complex containing a cysteine-sulfur atom as the sixth ligand ($-S-Fe^{II}-O_2^-$ radical)[70]. The oxygen is here so basic that it deprotonates fluorene[71]. Other mechanisms are, however, provisionally not excluded[72].

The attempts to imitate the catalytic activity of the heme enzymes *in vitro* by means of metalloporphyrins have been lamentably unsuccessful. Only radical chain peroxidations occur, as for example in the reaction of cyclohexene *(12)* illustrated, this being catalyzed by some metalloporphyrins[73, 74]. Such reactions are, however, catalyzed by innumerable metal complexes; a peroxide formed primarily is decomposed and probably no "oxygen activation" is involved, so that the expensive heme analog has been wasted.



(12)

Catalysis by bismetal systems in which the oxygen molecule is twice bonded and polarized is at the moment the most hopeful route. For example, a pair often used in biology is heme and copper ions bonded to a protein.

10. Prospects

The central problems for the future in this field are the synthesis of suitable molecular complexes of chlorophyll and porphyrins for conversion of light into redox energy (~membrane potential) and for specific catalytic oxidation of organic substrates by molecular oxygen. Both these problem areas are of extreme interest both scientifically and, in principle, for industry. Among specific starting points the following possibilities appear: syntheses and photochemical investigations of hydrated magnesium-porphyrin dimers (see Sections 3 and 6), construction of photoelectrodes from monomolecular porphyrin layers or aggregates with micellar double layers[48] (see Section 6), and synthesis of porphyrins with intramolecularly defined ligand fields as well as covalently fixed electron-donors (see Section 9). These problems are currently under worldwide study and important progress may be expected in the near future.

In conclusion, let us return to *Pauling*'s remarks cited at the beginning of this review. Investigations to determine structure and syntheses of specific molecular complexes do not, of course, provide any "penetrating and reliable theory of weak interactions", but, in accord with one of the valued traditions of organic chemistry, they enable general rules to be derived and from these rules, prognoses. Specifically, complex systems of varied utility may thereby be obtained.

"What the chemist does in a situation like this is to analyze many molecules of a similar kind and get some empirical rules. It is not very satisfactory from the point of view of a physicist who is trying to understand from first principles. But the problem of the chemist is different. He must try to guess ahead of time what is going to happen with molecules that haven't been made yet, or which aren't understood completely ... (Don't forget that the reason a physicist can really calculate from first principles is that he chooses only simple problems)[75a] ... and lo and behold!, the chemists are almost always correct"[75b].

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Processing of Plastic Waste and Scrap Tires into Chemical Raw Materials, Especially by Pyrolysis[**]

By Hansjörg Sinn, Walter Kaminsky, and Jörg Janning[*]

Dedicated to DECHEMA on the occasion of its 50th anniversary

An account of the occurrence of pyrolyzable material and the state of development of pyrolysis processes in the USA and Japan is followed by a description of laboratory and pilot-scale experiments designed to exploit the raw material content of pyrolyzable substances rather than the heating value. Plastic waste and scrap tires can be pyrolyzed to give up to 40% by weight of aromatic compounds in fluidized sand beds which are surprisingly insensitive to the unit size of the feed material.

1. Motive for the Investigations

"If man had found huge heaps of a gray-white powder with the average composition of today's plastic production instead of crude oil and coal deposits, a chemical industry would undoubtedly have developed on the basis of this material". This insight, mentioned in an application to the Max-Buchner-Forschungsstiftung in 1969, has motivated our investigations into pyrolysis of plastic waste.

In 1973 6.4×10^6 tons of plastics were produced in the Federal Republic of Germany (FRG) and 5.1×10^6 tons were consumed, 1.0×10^6 tons of which were used as packaging materials. The total amount of waste plastics in the FRG was 1.4×10^6 tons in 1973, of which 1.0×10^6 tons were domestic or similar industrial waste. 700000 tons of this waste was short-life packaging. The weight-percentage of plastic in domestic waste fluctuates between 3 and 5 %, and the volume-percentage between 10 and 15 %. 135000 tons of waste comes from the production of the plastics producing and manufacturing industries. PVC, which comprises 0.6 wt-% of domestic waste, causes almost half of the HCl emission arising from domestic waste incineration. It was predicted that the volume of scrap tires for 1974 would total 340000 tons, of which 200000 tons require disposal[1].

As long as 90 % of world crude oil production is used for generating energy, the incineration of worn-out and used products of crude oil will continue to compete with all other utilization methods. For instance, the plastic material in domestic waste significantly raises its calorific value. The data from the Frankfurt municipal waste incinerator (Fig. 1) show a distinct reduction in calorific value because of a 6% drop in plastic production[3] in 1974. Existing waste incineration plants are designed for a definite calorific value of the feed. Increased calorific values because of greater proportions of plastic material in the waste causes localized reductions in the incinerator and therefore limits the throughput of the plants. A fundamentally different situation would arise, if a lower percentage of crude oil were used as fuel material. Nevertheless, in the FRG the weight production of plastics is equivalent to the amount of its crude oil production. Remarkable in this context is the fact that the Middle East extracts a yearly 400000 tons per rig; on the other hand the FRG only extracts approximately 2200 tons and the USA an average of 1200 tons per rig per annum. Furthermore the cost of land drilling in the USA or the FRG is approximately 500000 DM per drill[4]. Clearly, even small pyrolysis plants would be economically viable at the present time if

1) the pyrolysis products were comparable with or superior to crude oil,
2) the costs of investment did not exceed 500000 DM per 1000 tons per annum,
3) the process were self-supporting in energy, and
4) the running costs were equivalent to those of oil rigs.

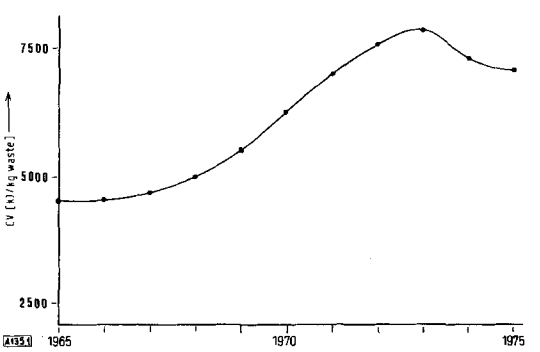

Fig. 1. Change in calorific value (CV) of refuse burnt in the Frankfurt municipal incineration plant (see [3]). There was a constant rise in the calorific value until 1973, and since 1974 it has decreased by around 9 %. In the first half of 1975 it had not yet increased. The reason for the decrease is not easily explained. However, it is certainly related to the decrease in plastics production (about 6% from 1973 to 1974) and the 25% decrease in 1975 in paper sales.

We know today that conditions 1 and 3 can be met. The fulfillment of condition 2 seems to be possible. Information is not yet available for a decision on condition 4; the feed costs are a decisive factor, because of the unknown expense of the separation process required to provide a feed consisting almost exclusively of plastics.

Numerous pyrolysis plants have been developed for processing unseparated waste to save on separation costs and aiming specifically at conversion into energy. An excellent survey of these processes together with a list of the original publica-

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tions is given in the conference paper "Conversion of Refuse to Energy"[2].

A comparative study of the waste incineration and pyrolysis processes by *Tanner*[5] comes to the following conclusions: One of the major advantages of pyrolysis is the minimization of gas production. All gas-containing components, especially the dust precipitators can be smaller than in incineration plants. An additional advantage seems to be that the energy obtained turns out to be storable, although it is still debatable whether this advantage justifies the installation of the process. The necessity of crushing the feed prior to pyrolysis is seen as a disadvantage.

Inoffensive and hygienic disposal is *Tanner*'s main preoccupation, economic aspects being of secondary importance. The following assumptions are made concerning the present state of development (see Table 1): In the near future the classical incineration processes will be improved; on the other hand the various pyrolysis processes present a new and interesting approach, but it will take another five to eight years before their effectiveness can be definitely assessed.

reactor, hot particles of char provide the energy needed to pyrolyze the organic material. The char, which is actually the solid residue of the pyrolysis reaction, enters the reactor after having been heated to a temperature of 760°C and is mixed turbulently with the organic material. Five parts by weight of char will be mixed with each part of organic material. The pyrolysis reaction takes place as the char-waste mixture proceeds through the reactor. The organic feedstock is broken down into a gas and char mixture. Because this reaction is endothermic, the temperature of the mixture will fall to about 510°C by the time it leaves the reactor.

A mechanical separator or cyclone is used to remove the char from the gas. The char which now consists of the char fed into the reactor as well as that newly formed by the pyrolysis reaction, is stored for re-use in the reactor. Before being recirculated to the reactor, this stored char is reheated. Excess char is removed for disposal in a sanitary landfill.

The process gas that has been separated from the char will be cooled quickly to 80°C in an oil decanter. In this device, oil is sprayed into the gas stream, causing it to cool.

Table 1. Principal pyrolysis processes for waste materials, their status of development, and their advantages (see [5]).

Designation	Process	Advantages [a] A	B	C	D	E	F	G	Pilot plants	Full scale plants under construction	Ref.
Destrugas	Gas extraction in a shaft furnace, uniflow	+	+	+			+		Kalundborg (DK) 5 t/d		[8]
Garrett	Gas extraction in a retort	+	+	+	+		+		La Verne, Calif. (USA) 4 t/d	San Diego, Calif. (USA) 200 t/d	[7]
Sodeteg	Gas extraction in a shaft furnace, uniflow	+	+	+			+		Grand Quevilly (F) 12 t/d		[44]
Warren Spring	Gas extraction in a shaft furnace, uniflow	+	+	+	+		+		laboratory test		[45]
Dr. Fink	Gas extraction in an electric arc furnace	+	+	+		+		+	study stage		[46]
Prof. Weiss	High temperature and pressure, catalyst	+	+	+	+		+		laboratory test		[5]
2-Stage incinerator	Two stage incineration	+	+				+		laboratory test		[47]
Landgard	Vaporization in a directly heated rotary furnace, countercurrent	+	+	+					St. Louis, Mo. (USA) 35 t/d	Baltimore, Md. (USA) 1000 t/d	[48]
Lantz	Vaporization in a direct heated rotary furnace	+	+	+					San Jose, Calif. (USA) 40 t/d		[46]
Purox	Vaporization with pure O_2, shaft furnace, countercurrent	+	+	+		+			Terrytown, N.J. (USA) 5 t/d		[49]
Andco-Torrax	Vaporization with hot air, shaft furnace, countercurrent	+	+	+		+			Buffalo, N.Y. (USA) 75 t/d	Luxembourg 200 t/d	[50]
US Bureau of Mines	Pyrolysis under pressure, with CO catalyst	+	+	+	+		+				[51]
West Virginia University	Fluid bed reactor	+		+			+		Morgantown, W.Va. (USA) 1 t/d		[52]

[a] A, small quantities of gas; B, little dust; C, generation of gas; D, production of oil; E, insoluble slag; F, metals not oxidized; G, ferrous metals recovered.

Comparison of a fuel oil with the pyrolysis oil of the San Diego plant and the liquid fraction obtained on fluidized bed pyrolysis of a representative mixture of thermoplastic material is of interest in this context. The pyrolysis oil from unseparated waste is seen to be relatively highly oxidized (see Table 2).

The more demanding pyrolysis processes require a relatively sophisticated feed preparation. The Garrett process for instance utilizes two shredders and two-stage air classification. The actual pyrolysis step is described by *Levy*[7] as follows: The pyrolysis reactor is a vertical stainless steel pipe through which the organic feedstock is blown pneumatically. In the

The cooling must be done very quickly to stop the chemical reactions taking place in the gas and thus prevent a reduction in the yield of fuel. The oil used for cooling is a combination of the liquid fuel produced by the plant and No. 2 fuel oil. After cooling, the liquid fuel settles in the base of the decanter.

The remaining gas stream is subjected to a series of clean-up steps and then compressed. Part of this gas will be used as the oxygen-free medium for pneumatically transporting both the organic feedstock and the char into and through the pyrolysis reactor, and the remainder is used for energy production. It is useful to bear in mind the differences and similarities between the above process and the fluidized bed

Table 2. Typical properties of fuel oil and pyrolytic oils.

Composition [wt-%]	Fuel oil [a]	Oil from pyrolysis of waste materials [b]	Oil from pyrolysis of a mixture of plastics [c]	Oil from pyrolysis of scrap tires [d]
C	85.7	57.5	83.48	88.0
H	10.5	7.6	7.85	8.5
S	0.5—3.5	0.1—0.3	—	1.15
Cl	—	0.3	5.97	—
O, N	2.0	33.4 0.9	— —	
Ash content [wt-%]	0.5	0.2—0.4		< 0.01
Calorific value [MJ/kg]	42	24	40	41
Specific gravity [kg/l]	0.98	1.3	0.891	0.980
Pour point [°C]	18—30	32	< −20	− 4
Flash point [°C]	66	57	< +20	< +10
Viscosity [cSt]	18—55	215	11.4	10.6

[a] No. 6 fuel oil [6].
[b] Garrett R+D Comp., San Diego, Calif. (USA) [6].
[c] The model mixture consisting of 7 parts by weight of polyethylene, 2 poly(vinyl chloride), 2 polystyrene, 1 polypropylene was fed into the laboratory test plant at the University of Hamburg, Germany; test specifications DIN.
[d] Oil product gained with the prototype reactor at the University of Hamburg (see Figs. 9 and 10). The inadequate cooling system only gave an oil consisting mainly of compounds with higher boiling points whose properties are given here. Chemical analysis given in Table 6; test specifications DIN.

process for the pyrolysis of plastics which is discussed later in the paper.

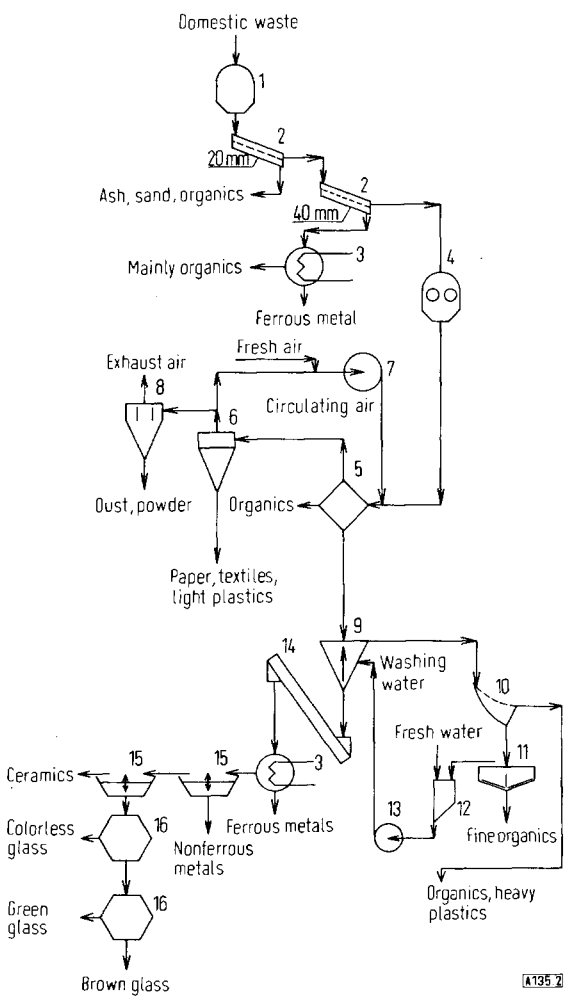

Fig. 2. The flow scheme of the domestic waste separation plant at the Technische Hochschule Aachen (see [12]). 1, feed precrusher; 2, fine sieve; 3, magnetic separator; 4, cutting roller mill; 5, air classifier; 6, cyclone; 7, ventilator; 8, dust separator; 9, fluidizing classifier; 10, water separation sieve; 11, thickener; 12, bottom product; 13, pump; 14, discharge and water separation system; 15, specific gravity separator; 16, optical-mechanical separator.

Opposing processes of this kind are those which need no feed preparation. The Destrugas process[8] for example heats up the unsorted waste in externally heated retorts. 500 m^3 of gas is produced per ton of waste, two thirds of which is used for maintaining the heat of the process. About 150 m^3 of gas can be given off; its constituents are: H_2 55%, CH_4 10%, hydrocarbons 2%, CO 11%, CO_2 18%, and H_2O 4%.

According to experience gained in preparing waste for pyrolysis processes, the problem of separating waste into its component parts can be regarded as solvable. However, these processes are economically sound only if a number of valuable substances or their basic constituents are separated out before pyrolysis. In Franklin, Ohio, the 150 t/d *Black Clawson* process[9] involves a wet pre-separation of materials similar to the technology known from paper mills. A comparable process is the *Krauss-Maffei* R 80 process[10]: From the light weight part of the waste material the paper is "dissolved" in a kind of pulper and the plastics and textiles remain separable in the form of a "plait", which could be the supply for pyrolysis processes.

The *Bureau of Mines*, USA, operates a pilot plant dry process to separate waste into its components. Rotary mills and air classifiers are combined and an electrostatic precipitation of plastic material is being experimented with [9, 11]. *Hoberg*[12] at the Technische Hochschule Aachen has improved the process by incorporating liquid filled flow and gravity classifiers (see Fig. 2).

An additional source of feed for pyrolysis processes is provided by scrapped cars, with their relatively high proportions of plastic material. In 1973, 3643000 sedan cars with an average weight of one ton each were produced in the FRG. They will have to be scrapped at some point. In each ton there is about 250 kg of plastics, glass, rubber, textiles, and cardboard which are easy to separate. This gives a total amount of one million tons of non-metal material a year, which is on the increase. At present this material is granulated and dumped.

Furthermore a considerable amount of plastic material (some 10000 t/a) comes from scrap wiring material. At present the copper core is regarded as the more desirable material,

and the plastic or rubber insulation is just burnt off in retort furnaces (an antediluvian process) with considerable emission of HCl gas. Mechanical stripping processes are also available for separating the metal and the insulation, but the dumping cost for the insulating material reaches 40 DM/ton.

Oda et al.[16] developed a process that dehydrochlorinates plastic waste with a content of 20 wt-% of PVC at 280 to 300°C with retention times of 40 minutes, the HCl gas produced being dissolved to form hydrochloric acid. The char produced by this process and the rest of the remaining non-

Table 3. Composition of pyrolyzable waste and scrap material (data from Northrhine-Westphalia, FRG) (see [14]).

	Amount [t/a]	Calorific value [kcal/kg]	Composition [%] organics	water	sulfur	chlorine	metal	SiO_2 *etc.*	Delivered in
Industrial waste similar do domestic waste									
Trade waste		3400	64	10	—	1	1	24	A, F
Solid special waste									
Plastics without PVC [a]	20000	6500	80	—	—	1	5	14	A, B, C, E
PVC [a]	3000	4500	42	—	—		57	1	A, B, C, E
Chemical waste, varnish, paint	20000	5500	42	20	25	2	1	10	B, C, D
Rubber (excluding scrap tires)	2000	4500	65	—	25	10	—	—	A, B
Scrap tires	87000	6700	69	—	19	1.5	—	10.5	E
Bitumen	15000	5200			—	—	—		B, C
Bleaching and filter earth	20000	4000	45	3	—	2	—	50	B, E
Binder, pigments	5000	2500	37	10	—	1	2	50	B, C
Car shredder waste	40000			—				—	A, E
Used cabling	20000	1700	15	—	70 [b]	—	15	—	E
Pastes									
Acid catalysts from waste oil refinery	40000	4800	45	20	—	15	—	20	
Acid catalysts from oleum plants	5000	2100	35	15	—	24	—	26	
Waste heavy oil	20000	4000	42	30	—	3	—	25	
paint and varnish waste	1000	7800	98	—	—	2	0.2	—	
Liquid waste									
Waste oil	150000	8700			—		—		C, F
Oil sludge	100000	5500			—		—		C, F
Solvents	80000	8300		—	—		—		C, F
Paint sludge	15000	2500			—		—		B, C, F
Toxic Waste									
Chromium contaminated sludge	3000	—	—	85	15	—	—	—	

[a] Considerable amounts are present in trade waste-like packaging *etc.*
[b] Content of copper 50%, others are lead, steel, and aluminum.
[c] A, container; B, trough; C, drum; D, bottles; E, trucks; F, road tanker.

Finally it should be noted that the Funabashi project has proved the feasibility of separate collection of waste[13]. A list of pyrolyzable waste material produced in Northrhine-Westphalia is shown in Table 3[14].

2. Pyrolysis of Separated Plastic Material

Almost identical decomposition graphs were reported for relatively long retention time in the pyrolysis zone (>20 minutes) by *Matsumoto et al.*[15] and *Oda et al.*[16] (Fig. 3 and 4).

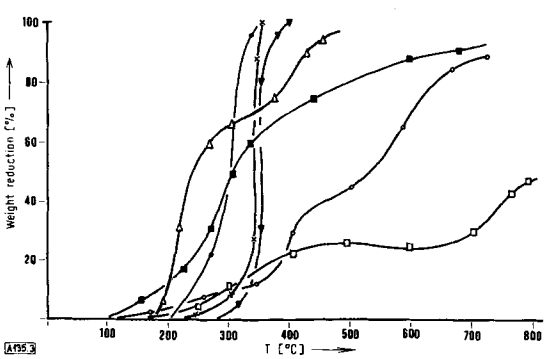

Fig. 3. Thermal decomposition characteristics (see [15, 16]). ●, polypropylene; ×, polyethylene; ▼, polystyrene; △, PVC (hard type); ■, urea resin; ○, phenol resin; □, polyester.

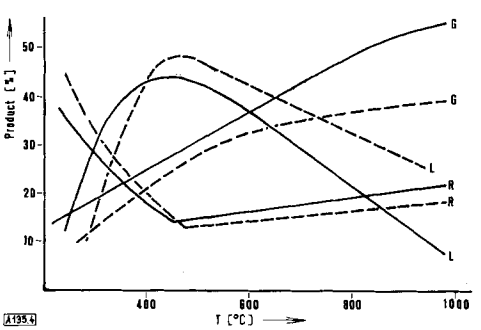

Fig. 4. Product composition *vs.* decomposition temperature (—·— retention time 1.5 h, ---- retention time 0.5 h); G, gaseous products; L, liquid products; R, residue (see [15]).

decomposed plastic material is burned with excess air in an incinerator. The combustion gases leave a Venturi scrubber with *ca.* 10 ppm HCl, up to 50 mg Pb per normal cubic meter, and 0.8 mg Cd per normal cubic meter. The waste water goes through a coal filter with a pH of 7.8, <0.01 ppm cadmium, and 0.1 ppm lead. A 5 t/d pilot plant was constructed in 1973 in Koshigaya city. The plant meets the requirement that water and air pollution be avoided.

Kitaoka et al.[17], *Shimizu et al.*[18], and *Speth*[19] have proposed essentially the same method for manufacturing a fuel oil (used on site) from the waste arising in polyethylene production. The waste is decomposed in externally heated agitator

vessels at 420 to 455°C, whereupon almost 90 wt-% of the feed is converted into oil with a gross calorific value of 11000 kcal/kg plus 5 % of C_1 to C_4 hydrocarbon gases. The amount of char produced is low. The processes are characterized by long residence times and recycling of hydrocarbons having high boiling points to the reaction vessel. The Japanese plant which processes one ton per hour has been running since 1971; operating data are available as well as running costs. The average energy needed for pyrolysis is 200 kcal/kg. The total costs are 22000 yen per ton (*ca.* 74 $/ton), but calculating the profits from the oil produced on the one hand and the savings on dumping costs on the other there is an overall profit of 650 yen per ton (*ca.* 2 $/ton).

Matsumoto et al.[15] have shown that it is preferable to process plastic material containing PVC in two stages, *viz.* prior dehydrochlorination and the gasification of hydrocarbons at a higher temperature. A semi-commercial pilot plant was built in 1971 and has a capacity of 100kg/h. Figure 5 shows a flow diagram of this plant. The feed material is treated in a melting vessel 8 at about 300°C. The chlorine present in the PVC is liberated mainly as HCl gas and is condensed by an absorption process 14. The molten plastic material is then fed into decomposition vessel 9 containing a cracking zone and a reflux zone. The former is kept at a constant temperature of 400 to 500°C depending on the kind of material. Forced circulation of the molten plastics is necessary for an even temperature distribution within the vessel. The temperature of the reflux zone is adjusted to ensure return of the waxy components to the cracker and to keep the gaseous products to a minimum. Typical test results are shown in Table 4. The economic minimum size of a commercial plant should be approximately 20 tons per day for industrial plastic waste, and 50 tons per day for municipal plastic waste.

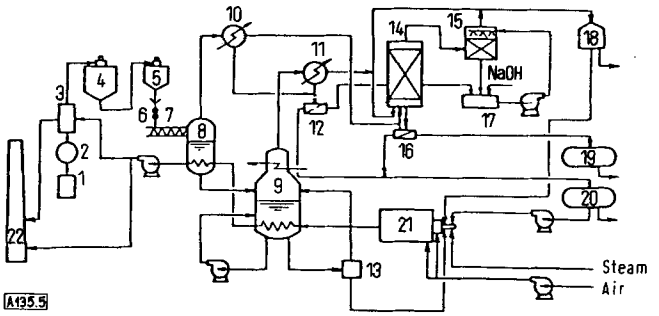

Fig. 5. Process flow diagram of the two stage plant of *Matsumoto et al.* (see [15]). 1, waste plastics; 2, crusher; 3, dryer; 4, storage tank; 5, feed hopper; 6, rotary valve; 7, screw feeder; 8, melting vessel; 9, thermal decomposition vessel; 10 and 11, condensers; 12, oil separator; 13, take-out device for decomposition residue; 14, absorption tower; 15, neutralization tower; 16, oil separator; 17, alkali tank; 18, gas holder; 19, hydrochloric acid tank; 20, recovered oil tank; 21, furnace; 22, chimney.

One hundred tons of domestic refuse produces 160 to 170 tons of steam (at 300 to 350°C) which will crack about 80 tons of industrial waste into fuel oil after being superheated to 500 to 650°C. The amount of fuel necessary for superheating this amount of steam is only about seven tons of oil. A one ton per day pilot plant for the processing of foam polystyrene by using superheated steam has recently been completed. Attempts to regain the basic compounds of polyurethane foam, polyamide and polyester, by hydrolytic decomposition also warrant mention in this context (see Section 6).

A five tons per day plant, which has been operated by Jacult at Yoga since 1974, uses the Fluid Cracking Process developed in Japan[23] (cf. the scheme in [21]). A sand cracker with a diameter of one meter is heated by partial combustion

Table 4. Typical test results with pilot plant run by Mitsubishi Heavy Industries (see [15]). Polypropylenes (1) and (2) are the atactic and isotactic froms.

Materials processed	Product composition [wt-%] Gas	Oil	HCl	Yield [%]	Characteristics Flash pt. [°C]	Visco-sity [cSt]	Pour pt. [°C]	Ash [%]	Sulfur [%]	Spec. wt.	Cal. value [kcal/kg]	Mois-ture [%]
Polypropylene (1)	1.8	97.1		98.9	−15	1.21	< −40	<0.01	<0.01	0.766	10.960	<0.1
Polypropylene (2)	4.3	95.0		99.3	−15	1.10	< −40	<0.01	<0.01	0.766	11.170	<0.1
Polypropylene 50 % Polystyrene 20 % Polyethylene 30 %	5.4	93.8		99.2	−30	1.16	< −40	<0.01	<0.01	0.802	10.620	<0.1
Polypropylene 75 % Phenol 25 %	5.3	82.9		88.2	− 6	1.46	< −40	<0.01	<0.01	0.778	11.270	<0.1
Polyethylene 75 % PVC 25 %	1.1	71.6	10	82.7	3	1.42	− 4	0.03	<0.01	0.782	11.680	<0.1
Mixture [a]	11.9	73.2	7.7	92.8	2	1.33	− 4	<0.01	<0.01	0.796	11.210	<0.1

[a] Composition: Low density polyethylene 35.7%; high density polyethylene 14.2%; polypropylene 10.8%; polystyrene 16.9%; PVC 18.0%; other components 4.4%.

Similar investigations by *Tsutsumi*[20] were published earlier[21]. The use of microwave heating to melt and to preseparate HCl should again be noted. The actual pyrolysis reactor is an externally heated screw chamber. Interestingly, *Tsutsumi* now doubts that the process will be economically feasible[22]. His remarkable new proposal is a pyrolysis process using superheated steam at 500 to 650°C generated in waste incinerators (see Fig. 6).

of the feed material to 350 to 600°C for the decomposition of non-returnable polystyrene bottles.

Some 80 to 85 wt-% of the feed material is transformed into oil in a plant with an energy requirement of 26 kW, a steam requirement of 500 kg/h, and a cooling-water requirement of 5 m^3/h. The oil has an average molecular weight of 176 and contains 1.5 % benzene, toluene, ethyl benzene, 62% styrene, and 30% di- and oligo-styrene, besides smaller

amounts of higher-boiling fractions. The investments costs for 1973 were one million DM[23]. The process is said to be applicable to other plastic materials containing up to 10

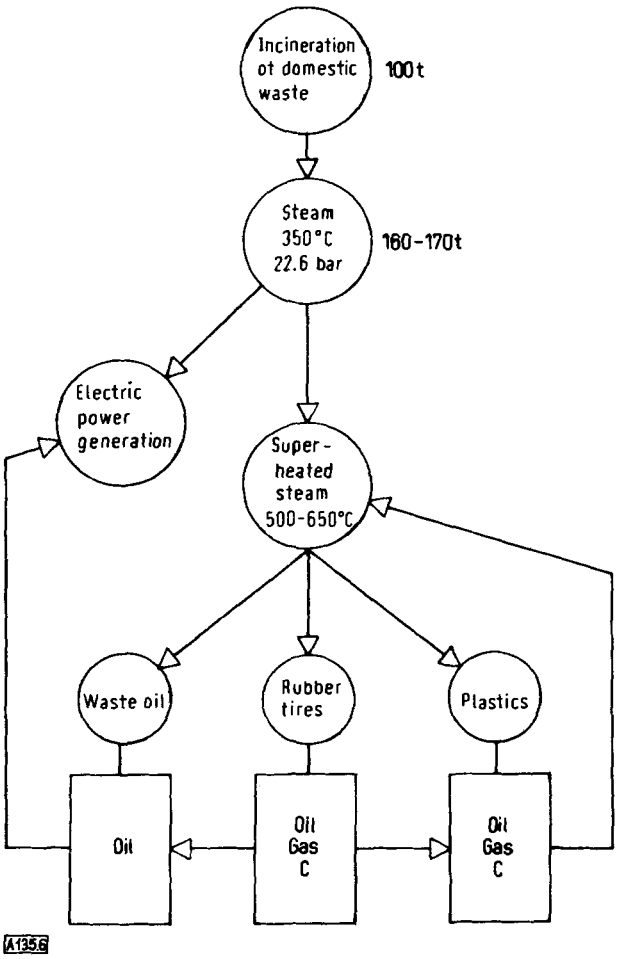

Fig. 6. Proposed future process for the recycling of industrial waste (see [22]). Pyrolysis products: 70 to 95% oil from waste oil; 40% oil, 20 to 25% gas and 30 to 35% carbon residue from scrap tires; 90 to 92% oil, 8 to 9% gas and 2 to 3% carbon residue from plastic material.

wt-% PVC and also to scrap tires. As a result of partial combustion, which of course has a favorable influence on energy requirements, the product oils contain oxidized compounds (calorific value 9510 kcal/kg, that of styrene 10060 kcal/kg).

A similar plant with a throughput of three tons of plastic per day was constructed in 1973 by Sumitomo Machinery and Shipbuilding Co.[24] in the Tshiba factory at a cost of 1.2×10^6 DM. During the test runs at 450 to 500°C about 75 wt-% of the feed material was converted into fuel oil. The sand fluidized bed is maintained by an air stream from uderneath and about 15% of the plastic material fed in must be burnt to produce the energy required for the decomposition. After cyclone separation of the char, the hot gaseous products are passed to a rectification column. Non-condensable gases are burned off and the combustion gases released into the atmosphere after washing out the HCl.

No fluidized bed pyrolysis processes are operated without oxygen in Japan. The alternative use of gases and oils produced by pyrolysis processes, apart from providing energy, does not seem to have been considered. Recycling in the sense of regaining basic materials is nevertheless being planned in future developments.

One special case is the pyrolysis process (10 kg/h) developed by the Osaka Municipal Technical Research Institute (OMTRI) in which dehydrochlorination of PVC at 300 to 350°C produces polyene compounds that can be transformed into ion exchangers[25].

A part of the research project "Conversion of Plastic Waste"[26] funded by the VKE is the hydrolytic decomposition of polyurethane and polyesters carried out by Bayer AG[53-80]. *Grigat*[27] showed that the hydrolysis of polyurethane in screw chambers by passage of steam leads to toluylenediamine (which can be reprocessed with phosgene into toluylene diisocyanate) and polyether, such as is synthesized from 1,2-ethanediol and alkylene oxide. Thus, in this hydrolysis process, the C atom introduced as phosgene on synthesis of the isocyanate is removed from the urethane as CO_2.

Current research in Hamburg is concerned with assessing the suitability of plastic scrap as a source of raw materials. After the conclusion of laboratory scale experiments[28,29] our research has become part of the VKE project "Conversion of Plastic Waste"[26,30]. *Menzel*[28] used a fluidized sand bed and *Perkow*[29] a molten salt reactor, each with a throughput of 0.1 kg/h for their investigations. The laboratory-scale apparatus for fluidized bed pyrolysis[31,21,28] is shown and explained in Figure 7.

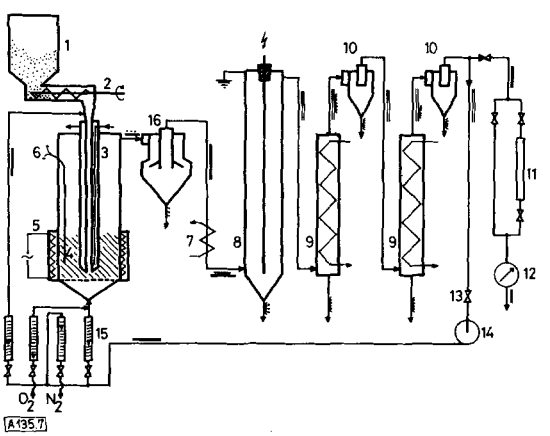

Fig. 7. Flow diagram of the laboratory test plant of fluidized bed pyrolysis by *Menzel* [28]. 1, plastic feed hopper; 2, screw conveyor; 3, downpipe with cooling jacket; 4, fluidized bed reactor; 5, cyclone 1; 6, cooler; 7, electrostatic precipitator; 8, intensive cooler 1; 9, cyclone 2; 10, intensive cooler 2; 11, cyclone 3; 12, gas sampler; 13, gas meter; 14, compressor; 15, rotameter.

Perkow's[29] molten salt reactor allowed sophisticated measurements of the amount of energy needed for the pyrolysis (Table 5).

Although the molten salt reactor has a lower energy requirement than the fluidized bed reactor, we decided, because of the corrosion and the higher build up of char residue, not to proceed any further with this research at present.

After we had been requested to construct a 10 kg/h pilot plant[30] we conducted experiments with a prototype reactor we named TPT. A conventional 110 liter garbage can was used, equipped with bent gas inlet tubes. To observe the principle of indirect heating and to avoid any pollution of the products, we used fire tubes inside the sand bed which had been developed by *Menzel*, *Kaminsky*, and *Tysarczyk* by scaling down the commercial tubes invented by *Schmidt*[32]

Table 5. Comparison of the measured and calculated data for the energy balance of the molten salt reactor. Pyrolysis at 690 °C (see [29]).

Feed material	Experimental values			Calculated values	
	Enthalpy of reaction at 250 °C [kcal/kg]	Heat removal [kcal/kg]	Energy consumption [kcal/kg]	Energy consumption [kcal/kg]	Difference [%]
Polyethylene	649	440	1089	1110	+1.9
Polypropylene	535	390	925	920	−0.5
Poly(vinyl chloride)	55	222	277	250	−9.7
Polystyrene	282	347	629	670	+6.5
Polymethyl methacrylate	163	375	538	580	+7.8
Mixture [a]	479	389	868	830	−4.4

[a] Composition: 7 parts by weight polyethylene, 1 polypropylene, 2 polystyrene, 2 poly(vinyl chloride).

Table 6. Mass and energy balances of the pyrolysis of plastic material [a, b].

Test conditions														
Feed material	PE/N_2						PE/SpG		PE/SpG/Kat		PSt			
Reactor	LWS		LSS		TPT [c]		LWS		LWS		LWS		LSS	
Temperature [°C]	740	840	740	850	740	840	740	830	690	790	640	740	640	740
Identified products														
Hydrogen	0.3	1.2	0.6	1.6	0.4	0.5	0.5	1.0	0.8	1.9	+	0.03	–	0.3
Methane	6.7	13.1	13.7	23.5	7.9	11.9	16.1	23.7	13.7	16.7	0.1	0.3	0.7	2.6
Ethane	3.5	5.1	6.8	4.8	4.8	6.6	5.3	3.8	5.9	4.1	0.02	0.05	0.1	0.4
Ethylene	33.8	44.7	22.0	26.8	30.1	32.9	25.4	27.6	16.9	10.9	0.3	0.5	0.9	2.2
Propane	+	+	0.5	0.1	1.2	0.8	+	+	+	0.7	+	+	+	+
Propene	21.8	13.1	12.4	4.5	19.3	19.9	9.3	3.8	8.5	6.4	0.01	0.02	+	+
Isobutene, butane	8.4	1.6	2.1	0.4	7.5	5.7	1.1	0.2	0.9	2.5	+	+	+	+
Butene	3.2	0.7	3.4	1.9	8.0	6.7	0.5	0.1	0.6	1.2	+	+	+	+
Butadiene	9.9	6.2					2.8	2.0	1.6	2.5	+	+	+	+
Isoprene	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Cyclopentene	+	+	+	+	1.2	0.7	0.5	0.1	0.2	0.8	+	+	o	o
Cyclo- and dicyclopentadiene	+	1.2	0.7	0.1	1.0	2.4	1.0	0.5	0.8	0.8	+	0.01	o	o
2,1-Dimethyl-1-heptene	o	o	o	o	o	o	o	o	o	o	o	o	o	o
Aliphatic compounds C_5—C_8	0.07	0.3	2.1	0.1	11.3	3.6	4.6	0.7	4.8	9.7	+	+	o	o
Aliphatic compounds $\geq C_9$	4.5	+	5.0	0.1	2.9	+	7.1	+	17.0	4.4	–	–	–	–
Benzene	0.05	5.2	7.3	11.3	3.0	6.4	12.2	16.2	3.2	7.4	0.2	2.1	3.3	13.8
Toluene	0.02	1.1	2.2	1.7	1.1	1.5	3.6	4.0	1.5	5.1	1.5	4.5	9.9	10.0
Xylene, ethylbenzene	0.01	0.04	0.3	0.2	+	+	1.1	0.6	0.5	2.3	0.5	1.2	4.0	2.8
Allyl- and propylbenzene	–	+	–	+	o	o	o	+	o	0.7	+	+	o	o
Styrene	0.04	0.2	0.5	1.0	+	0.3	1.1	2.9	0.5	0.6	79.8	71.6	63.6	41.4
α-Methylstyrene	–	+	–	+	o	o	o	+	+	0.4	1.7	2.6	3.2	1.8
Indan, indene	0.02	0.2	0.1	0.2	+	+	0.3	1.3	0.2	0.3	0.6	1.4	+	+
Naphthalene	0.02	0.7	1.3	3.0	0.3	+	0.7	2.7	0.07	0.8	0.1	0.8	1.4	4.4
Ethylnaphthalene	0.01	0.2	0.3	0.4	o	o	0.15	0.6	0.01	0.5	+	0.1	+	+
Diphenyl	+	0.09	0.2	0.3	o	o	0.02	0.3	o	o	0.01	0.2	0.4	1.3
Diphenylalkane	–	–	–	–	o	o	–	–	o	o	3.8	1.5	o	o
Acenaphthene, acenaphthylene	+	0.2	0.1	0.4	+	+	0.02	0.5	o	o	+	+	o	o
Fluorene	+	0.09	+	+	o	o	0.01	0.1	o	o	+	0.1	o	o
1-Benzyl-2-methyl-3,4-benzocyclobutene	–	–	–	–	o	o	–	o	o	o	5.0	0.05	o	o
Dimeric styrene	–	–	–	–	o	o	–	o	–	–	0.6	2.2	0.4	0.2
Phenanthrene	+	0.4	0.2	0.6	o	o	0.01	0.4	o	o	0.06	0.5	1.6	3.8
Anthracene	+	+	+	+	o	o	+	+	o	o	+	+	+	+
Methyl methacrylate	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Water	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Carbon monoxide	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Carbon dioxide	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Carbon residue	0.4	1.4	1.2	7.9	o	o	0.9	1.6	9.1	17.3	0.04	0.3	3.2	7.2
Σ gaseous hydrocarbon + hydrogen	87.6	85.7	61.5	63.6	79.2	85.0	61.0	62.2	48.1	46.9	0.4	0.9	1.7	5.5
Σ aliphatic compounds $>C_4$	4.6	1.5	7.8	0.3	16.4	6.7	13.2	1.3	22.8	15.7	+	+	o	o
Σ aromatic compounds	0.2	8.4	12.5	19.1	4.4	8.2	19.2	29.6	6.0	18.1	93.9	88.9	87.8	79.5
Pyrolysis products not mentioned above	o	1.3	4.2	3.7	o	0.1	o	4.5	0.2	o	4.7	6.3	5.0	1.2
Not identified by gas chromatography	5.8	0.6	10.2	3.5	o	o	5.1	1.9	11.3	o	0.1	0.2	0.8	6.3
Hydrogen chloride	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Hydrogen sulfide	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Fillers	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Balance	98.6	98.9	97.4	98.1	100.0	100.0	99.4	101.1	97.5	98.0	99.1	96.6	98.5	96.7

[a] Abbreviations: PE, polyethylene; PS, polystyrene; PVC, poly(vinyl chloride); PP, polypropylene; PMMA, poly(methyl methacrylate); MM, mixture of plastics: PE:PVC:PS:PP = 7:2:2:1 w/w; LWS, fluidized bed laboratory test plant; LSS, molten salt laboratory test plant; TPT, pilot plant prototyp; SpG, crackgas (not condensed gases); KAT catalyst (zeolite).

(see Figs. 8 and 9). Heat transfer (mainly radiation) to the feed material is therefore indirect with air excluded: the glowing tubes (steel 1.4876) are surrounded by fluidized sand and feed material.

The reactor was fed manually with plastic sticks weighing 20 g each *via* a cooled tube. Once we found that the heated fluidized bed is not adversely affected by pieces weighing even more than 1 kg, we constructed an air lock on top of a feed tube. An idea of the relative size of this part of the reactor can be gained from Figure 10.

The prototype reactor filled with 40 kg of very fine sand processes 20 kg of polyethylene or 15 kg of scrap tires per hour. The latter were introduced in pieces of up to 1.3 kg each (in a long experiment 0.7-kg pieces were fed in at 3-minute intervals). At present the pyrolysis gases are burned without any further treatment in an enclosed, low noise flue gas flare which has been placed at our disposal by BASF. Typical results of pyrolysis are shown in Table 6.

Earlier graphs[21] proving the dependence of the product composition upon temperature, especially in molten salt, warrant mention in this context. Figures 11 a to 11 d show the corresponding results of pyrolysis of polyethylene, polypropylene, polystyrene, and crushed scrap tires in a fluidized bed reactor.

In addition to the investigations mentioned above, *Janning* is carrying out pyrolysis experiments with added steam in

PVC				PP		PMMA		Scrap tire material						MM	
LWS		LSS		LWS	LSS	LWS	LSS	LWS		LSS		TPT/N_2 [c]		LWS	LSS
740	845	740	790	740	740	740	690	740	840	700	790	780	800	790	790
0.7	0.8	0.6	0.8	0.5	0.7	+	0.3	0.8	1.4	1.0	1.3	1.4	3.5	0.7	0.9
2.8	3.0	2.7	3.2	17.0	21.0	+	7.4	10.2	12.2	9.3	11.8	20.2	22.2	13.0	18.6
0.4	0.2	0.6	0.6	4.4	3.7	+	0.9	1.2	0.6	2.1	1.3	4.2	5.7	3.0	4.1
2.2	1.7	1.1	1.5	13.9	15.5	+	4.5	2.6	2.1	3.8	4.0	18.0	19.9	13.2	17.4
o	o	o	o	+	+	+	1.4	+	+	+	+	0.3	0.7	0.04	+
0.4	0.1	0.5	0.5	13.7	16.3	+	11.5	0.7	0.2	4.5	1.8	6.9	11.1	2.7	6.6
o	o	o	o	5.3	6.1	+	+	0.2	+	1.2	0.3	1.4	2.4	0.2	0.1
o	o	o	o	0.5	1.6	+	+	0.1	+	1.2	0.4	0.2	0.6	0.7	0.5
+	+	+	+	2.0		+	1.9	0.3	0.07			2.7	5.3		
–	–	–	–	o	o	–	–	0.1	0.05	0.4	0.1	o	o	o	o
o	o	o	o	0.7	o	+	o	o	o	o	o	o	o	0.1	o
+	+	+	+	2.5	0.2	–	o	0.08	0.1	+	+	+	+	0.4	+
o	o	o	o	0.4	0.1	–	o	o	o	o	o	o	o	o	o
+	+	+	+	13.2	0.1	–	o	o	o	o	o	1.4	1.7	0.8	+
–	–	–	–	2.7	+	–	o	o	o	o	o	1.7	+	1.8	–
3.5	4.3	4.0	4.3	10.4	8.6	+	1.5	4.2	5.9	2.6	4.3	18.3	11.5	14.7	8.7
1.1	1.2	1.2	1.6	5.7	4.6	+	1.0	3.8	3.3	3.4	2.9	12.0	7.9	4.5	3.2
0.2	0.2	0.3	0.2	1.8	0.8	–	+	1.9	1.1	1.9	1.0	2.9	3.1	0.9	0.6
–	–	o	o	o	o	o	o	o	o	o	o	0.4	o	0.4	o
+	0.1	0.1	0.1	0.9	0.7	–	–	2.3	2.3	0.7	0.8	3.8	3.1	10.5	4.1
o	o	o	o	o	o	o	o	o	o	o	o	0.6	0.3	+	0.1
+	0.4	0.2	0.2	0.5	0.4	–	–	0.8	1.0	0.4	0.4	0.5	0.2	1.3	0.6
3.1	2.4	2.0	2.5	0.4	2.3	–	o	0.9	1.9	0.8	2.2	2.1	0.8	2.5	3.7
1.2	1.0	1.0	0.9	0.1	0.8	–	o	0.7	0.9	0.7	1.0	0.9	+	0.5	0.7
0.8	0.6	o	o	+	0.3	–	o	0.3	0.4	0.3	0.5	+	+	0.3	0.6
–	–	o	o	o	o	–	o	o	o	o	o	o	o	0.2	o
+	+	o	o	+	0.2	–	o	0.2	0.4	o	o	o	o	0.1	o
0.4	0.5	o	o	+	+	–	o	0.1	0.1	o	o	o	o	0.2	o
–	–	o	o	o	o	–	o	o	o	o	o	o	o	o	o
–	–	–	–	–	–	–	o	o	o	o	o	o	o	0.1	o
0.6	0.8	0.7	0.9	+	0.3	–	o	0.08	0.3	0.1	0.5	o	o	0.4	1.1
+	+	o	o	o	o	–	o	o	o	o	o	o	o	0.1	o
–	–	–	–	–	–	94.0	25.8	–	–	–	–	–	–	–	–
–	–	–	–	–	–	+	0.4	0.4	1.2	o	o	o	o	–	–
–	–	–	–	–	–	+	19.0	+	+	o	o	o	o	–	–
–	–	–	–	–	–	2.0	18.3	+	+	o	o	o	o	–	–
8.8	8.6	9.8	12.1	0.9	0.9	1.0	1.6	42.8	45.5	38.3	48.6	o	o	2.9	5.6
6.4	5.8	5.5	6.6	57.3	64.9	+	27.8	16.1	16.6	23.1	20.9	55.3	71.4	33.5	48.2
–	–	–	–	19.5	0.4	+	+	0.2	0.2	0.4	0.1	3.1	1.7	3.1	+
10.9	11.5	9.5	10.7	19.8	19.0	+	2.5	15.3	17.6	10.9	13.6	41.5	26.9	36.7	23.4
16.3	17.3	3.7	4.3	0.5	5.3	–	–	5.2	2.5	6.8	2.0	0.1	o	2.6	2.5
		12.1	8.9	2.4	8.5	–	3.4	9.0	5.9	11.9	6.0	o	o	11.3	5.7
56.3	56.4	56.3	57.2	–	–	–	–	–	–	–	–	–	–	8.1	9.0
–	–	–	–	–	–	–	–	1.6	0.7	1.9	2.2	+	+	–	–
–	–	–	–	–	–	–	–	7.9	7.1	5.2	5.0	+	+	–	–
98.7	99.6	96.9	99.8	100.4	99.0	97.0	98.8	97.3	96.1	98.5	98.4	100.0	100.0	98.2	94.4

[b] +, trace detection; –, not present; o, traces possible, but not identified.
[c] Mass balance without carbon; component not identified by gas chromato graphy is not determined.

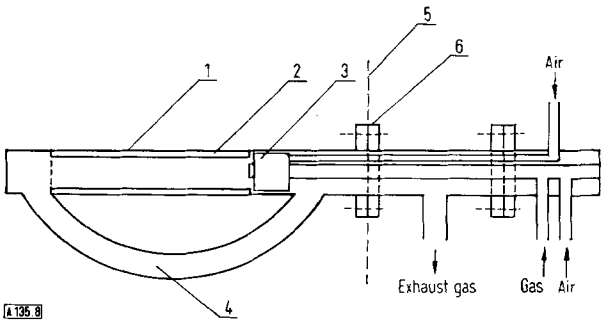

Fig. 8. Sectional drawing of the radiation fire tube installed in the prototype reactor (see Fig. 9). 1, radiation tube; 2, ceramic; 3, burner tip; 4, exhaust gas outlet; 5, reactor wall; 6, flanged connection.

a laboratory scale metal reactor. It has a noticeable effect on the composition of the products (see Fig. 12). The large amount of char is surprising. As we now know from comparable experiments in a quartz reactor, the pronounced char

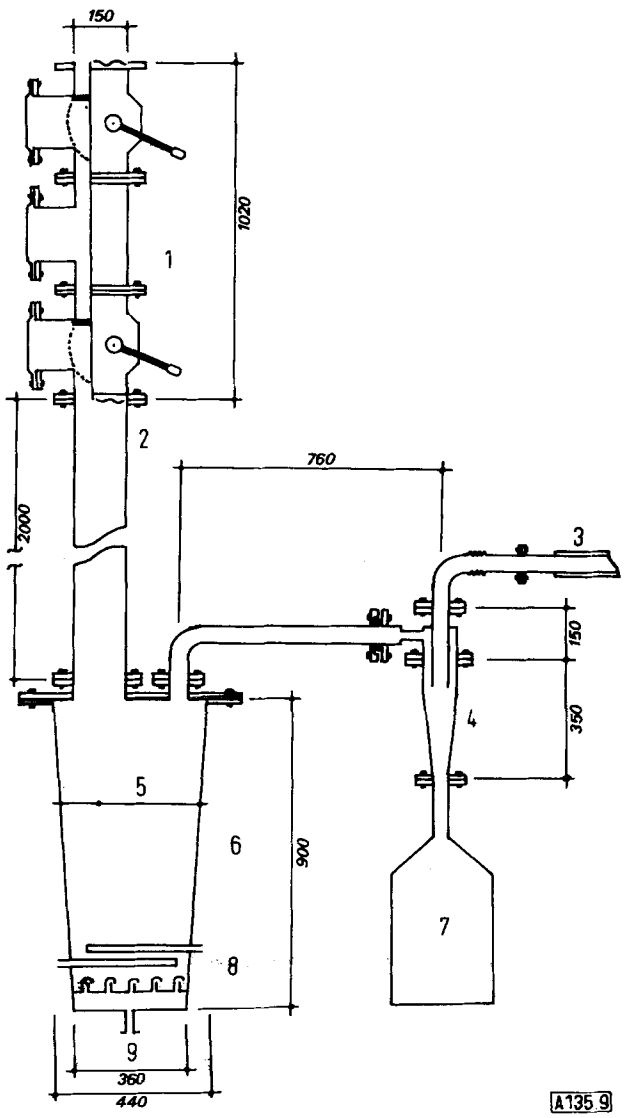

Fig. 9. The prototype reactor with feeding system for the pyrolysis of scrap tire pieces. 1, air lock; 2, downcomer; 3, cooler; 4, cyclone; 5, baffle; 6, fluidized sand bed reactor; 7, carbon black container; 8, fire tubes (see Fig. 8); 9, fluidizing gas inlet.

Fig. 10. Feeding of scrap tire pieces into the lock channel of the prototype reactor (see Fig. 9).

formation is caused by reactions with the metal wall. The investigations prove, on the other hand, the expected reduction of char by adding steam.

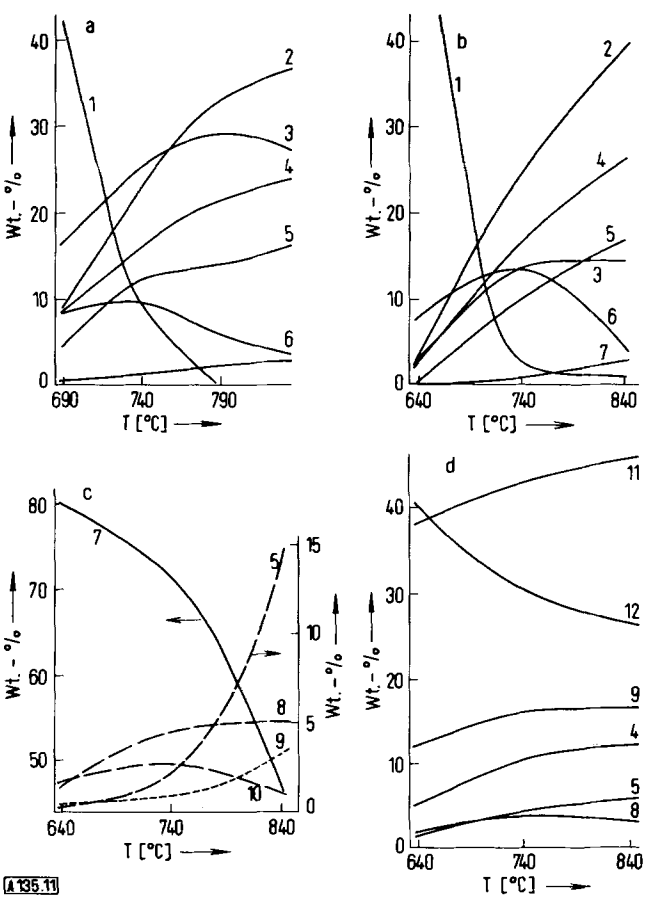

Fig. 11. Product composition of fluidized bed pyrolysis. Different plastics *vs.* temperature: a) polyethylene; b) polypropylene; c) polystyrene; d) scrap tire material; 1, Σ aliphatics ≥ C_9; 2, Σ aromatics; 3, ethylene; 4, methane; 5, benzene; 6, propene; 7, styrene; 8, toluene; 9, Σ gases: H_2 and C_1 to C_4; 10, α-methylstyrene; 11, carbon residue; 12, Σ pyrolysis oil.

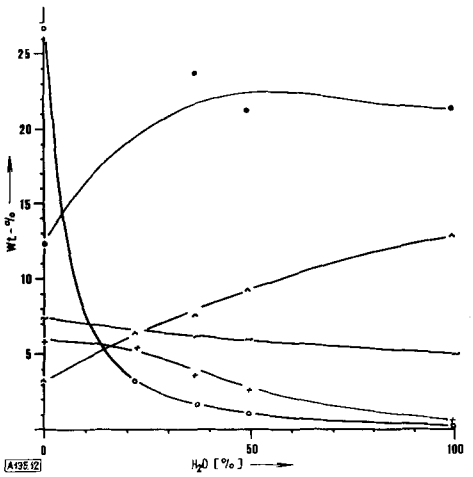

Fig. 12. Influence of steam on the composition of products of pyrolysis of polyethylene at 800°C. ○, carbon residue; ●, ethylene; ∧, propene; ~, benzene; ×, hydrogen.

3. A Pilot Plant

The preliminary experiments described above led to the design of a pilot plant whose overall layout is shown in Figure 13. Plastic material is pyrolyzed in a fluidized bed reactor utilizing quartz sand heated to about 800°C. The fluidizing medium is preheated pyrolysis gas and heating is maintained by radiating fire tubes in which either propane or pyrolysis gas can be burned. The feed enters the sand bed either at the top of the reactor through an air lock (ZR 1) or through a water-cooled screw feeder (ZR 2 with S 1) at the side.

of about 15° and carries the bent gas inlet tubes. These tubes are movable vertically so that their distance from the bottom of the fluidized bed can be varied. With this arrangement there is a variable settling zone for small metal pieces such as will be desposited on pyrolytic stripping of copper-cored wiring. A flanged inspection cover is fitted to the bottom of the gas distribution zone.

The pyrolysis gas produced is cleaned together with the fluidizing gas in a cyclone (Z 1); especially if the feed contains of scrap tire material, char and zinc oxide will be precipitated. The cleaned gas is led to the condenser (K 1) which is actually a vertical tubular heat exchanger. In the case of condenser failure, a three way cock allows the gas to be fed directly to the flare. The gas leaves the condenser (K 1) at 20 to 50°C, or at 100°C if the cooling capacity is reduced to avoid clogging by paraffin waxes. Condensed products collect in a receiver (G 1).

In a counter-current packed washer (K 2) the gas is then cooled to −20°C. The condensed products are dissolved in the scrubber oil and can be collected in a container (G 2). This container feeds the scrubber oil pump. For cooling the scrubber oil to −20°C a counter-current tubular heat exchanger (WT 1) is used. The liquid products collected are processed together with the scrubber oil in a glass rectification column.

The non-condensable components of the pyrolysis gas are compressed to 2 to 3 bar and stored in a gasometer. Fluidizing gas as well as fuel gas for the radiating fire tubes are tapped off as required. The fluidizing gas is preheated to 400°C in a counter-current heat exchanger (WT 2) by the exhaust gas of the four fire tubes.

The plant is equipped with numerous data-collecting instruments. Because we have deliberately separated the hot and

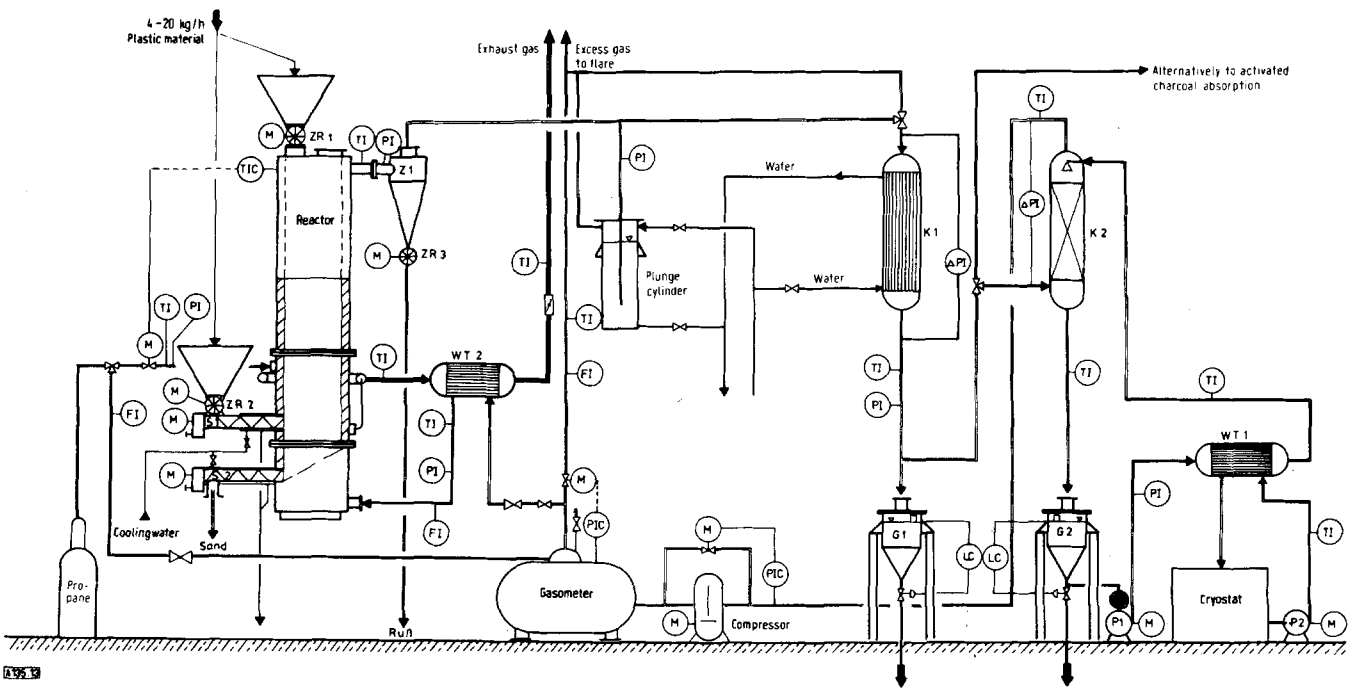

Fig. 13. The pilot plant at the Abteilung für Angewandte Chemie, University of Hamburg, Germany. PI, pressure indicating device; PIC, automatic pressure control; TI, temperature indicating device; TIC, automatic temperature control; FI, flowmeter; LC, level indicator; M, motor; WT, heat exchanger; ZR, bucket wheel lock; K, cooler; S, screw feeder; G, container; Z, cyclone; P, pump.

A water-cooled screw conveyer (S 2) is installed as an outlet for the quartz sand. At the top of the reactor is a safety bursting disc. The bottom of the fluidized bed has an incline

cold parts of the plant, the latter, together with the processing of the pyrolysis oil, are situated in an explosion-proof room. Surveillance is carried out by continuous analysis of

the room air as well as by explosion limit controls. The pyrolysis gas is analyzed automatically by a gas chromatograph every hour. Some basic components are continuously monitored by infrared spectroscopy.

Installation of the pilot plant in our institute necessitates all these safety precautions; at the same time it is of great didactic value. The plant is currently being installed by Claudius Peters AG.

4. Investigations on the Pyrolysis Reaction

A comparison of pyrolysis in a fluidized bed (with nitrogen or pyrolysis gas as fluidizing agent) and the molten salt reactor has been made by *Krebs*[33] (see Fig. 14). Experiments with recycled pyrolysis gas show a surprisingly high production of aromatic compounds. Decomposition experiments on particular mixtures gave a more or less additive spectrum of products; pyrolysis of a model mixture (in a ratio of polyethylene : polypropylene : polystyrene : PVC = 7:1:2:2 which is comparable with the composition of the plastics fraction of domestic waste), however, shows that the fraction of aliphatic compounds produced can decrease rapidly even at lower temperatures owing to interaction between the products. At 640 °C 2.0 wt-% of long chain hydrocarbons ($>C_9$) were found; in the absence of interaction 13.6 wt-% would have been produced.

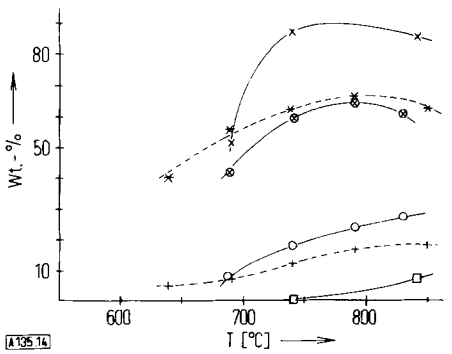

Fig. 14. Pyrolysis of polyethylene (compiled from [28, 29]). —— in fluidized bed reactor, --- in molten salt reactor: ×, Σ gases: H_2 and C_1 to C_4 (fluidizing medium: nitrogen); ⊗, Σ gases: H_2 and C_1 to C_4 (crackgas); ○, Σ aromatic compounds: C_6 to C_{10} (crackgas); □, Σ aromatic compounds: C_6 to C_{10} (nitrogen); *, Σ gases: H_2 and C_1 to C_4; +, Σ aromatic compounds: C_6 to C_{10}.

The surprisingly high and variable yield of aromatic compounds were examined in three further postgraduate investigations. *Krebs*[33] studied the decomposition of single polyethylene particles as a function of the temperature of the molten salt, the depth of immersion in the melt, and particle size by measuring the increase in pressure of the gas above the melt. The events observed after placing the particle on the surface of the melt can be described as follows:

The particle heats up immediately and softens but retains its round shape, at least until the end of the induction period [t_I] which is limited by the onset of the cracking. The explanation for the dependence of the induction time on the mass of the particle (t_I proportional to $m^{1/3}$) and the measurements of the temperature of the particle during decomposition correspond to the above observations (see Fig. 15).

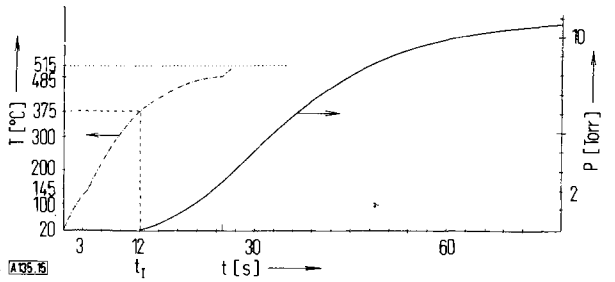

Fig. 15. Pyrolysis of single plastic particles in molten salt reactor (see [33]). Rise of the temperature in the particle and pressure in the reactor *vs.* time. ....., temperature of the melt; t_I, induction period.

Bock[34] studied the decomposition of single polyethylene particles in a sand bed "fluidized" by a vibrator, by monitoring the pressure arising as a function of time together with the temperature movement inside the particle.

The pressure *vs.* time graphs obtained in both studies show a typical S-shape. The induction time during the decomposition of a polyethylene particle of 2.5 mg drops from 8 to 0.8 s with a temperature increase of 515 to 725 °C. During this time, incipient cracking into long chain aliphatic compounds ($\geq C_{30}$) is observed.

One main difference between fluidizing bed and molten salt reactors consists in the actual reaction volume. In molten salt pyrolysis, the reaction volume of the gaseous products is essentially the gas layer between the polyethylene particle and the melt. As the volume of this gas layer and the amount of gas produced is proportional to the surface area of particle, the residence time changes with the temperature. The actual reaction volume in the fluidized bed is in fact greater than that in the molten salt; on the other hand the residence time of the gas produced is determined not only by the dimensions of the fluidized bed itself (diameter, height of expansion) but also by the gas penetration therein. This provides an explanation for the following observations:

1) The average molecular weights of the products in a simulated fluidized bed are considerably lower than those of the molten salt (and the real fluidized bed) because of the higher ratio of the amount of gas produced to the actual reaction volume and the consequent increase in residence time;

2) the drop in standardized final pressures (P_R/m) with increasing mass (m) because of a shortening of the residence time with increasing amounts of gas produced in constant volume.

The latter fact opens up the possibility of varying the residence times of the cracked products by feeding the fluidized bed reactor with different amounts of plastic per unit time. This could be used to achieve a desired composition of cracked products.

Finally *Döring*[35], using a 300-cm long fluid bed, which was divided into eight compartmentalized sections, took pyrolysis gas samples of the homogeneous sand/plastic mixture flowing down the tube in order to establish the relationship between the composition of the pyrolysis products and time. A significant result is shown in Figure 17.

In accord with the above three investigations the following picture emerges:

1) Polyethylene particles with a diameter of 0.5 to 0.8 mm melt in less than 0.2 seconds and the surface of the globule formed is covered with hot sand grains. Larger particles release

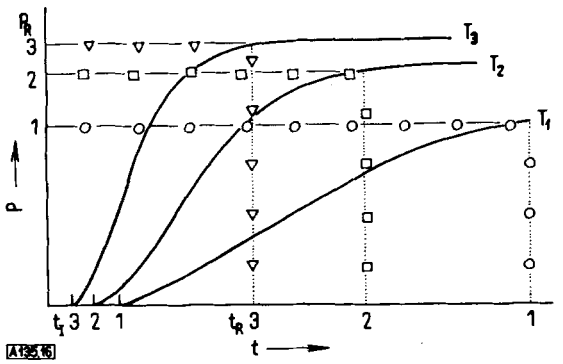

Fig. 16. Standardized pressure curves (see [34]). Pyrolysis of polyethylene at different temperatures ($T_1 < T_2 < T_3$); t_i, induction period; t_R, reaction time; P_R final pressure.

globules from their surface layer according to the amount of heat input.

2) As the temperature of the molten layer increases, pre-pyrolysis to long chain aliphatic compounds (C_{25} to C_{40}) takes place at 300 to 350 °C in the globule.

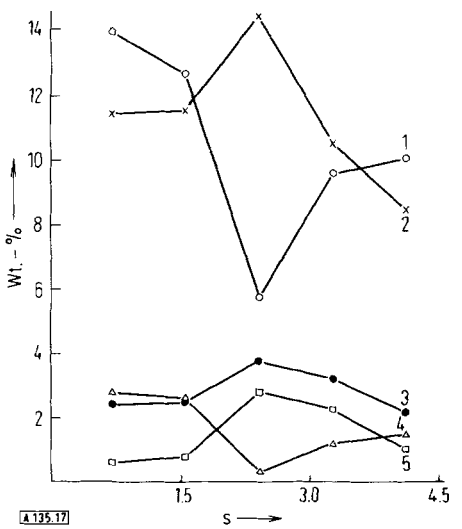

Fig. 17. Pyrolysis of polyethylene in a flow bed reactor at 700 °C (see [35]). Composition of each gas sample depending on the retention time of the granulated polyethylene feed. Retention times shown (1.5, 3.0, and 4.5 seconds) correspond to reactor lengths of 1, 2, and 3 m. 1, benzene; 2, propene; 3, butadiene; 4, toluene; 5, isobutene.

a) A postcracking of these aliphatic compounds occurs as the hot sand grains move onto free sites on the surface of the partially globulized particle. This produces, *inter alia*, C_3 and C_4 olefins which react in the gas/particle interface with its high concentration and temperature to form aromatic compounds with release of hydrogen.

b) Through the shearing force in the fluid bed, an "exchange" of sand grains takes place at the surface of the globulized plastic. Small amounts of the thin molten boundary layer are still attached to the sheared off particles, which are pyrolyzed by collision with hotter sand grains. The compounds thus produced are aliphatic ones or olefins. Of the latter, the C_3 and C_4 compounds form aromatic compounds in the laminar interface which also has a high temperature and high concentration. The gas experiences a relatively long residence time in the interface.

3) After further heating and pre-pyrolysis the globules disintegrate owing to volatilization of the low molecular weight compounds produced and to the shearing forces mentioned. The particles collide with hot sand grains and are cracked. The high gas production leads to shorter residence times of the products in the laminar interface and hence to cooling. Consequently, the amount of aromatic compounds produced drops, as does the post-cracking of the long chain aliphatic compounds. The amount of aliphatic compounds produced therefore increases at the end of the fluid bed.

4) Relatively cool sand grains with a layer of melted plastic on their surfaces collide with hot sand grains and the events described in 2) take place.

From these experiments it can be deduced that the spectrum of products can be varied according to the particle size of the feed, even in full-scale plants. A high yield of aromatic compounds results from high local concentrations of C_2, C_3, and C_4 olefins. This was proved directly by adding these gases during the pyrolysis in the laboratory test reactor as well as by feeding large pieces into the pilot plant reactor.

5. Pyrolysis of Scrap Tires

Pyrolysis of scrap tires has frequently been mentioned above. *Schnecko*[36] has recently published a review on it. At the moment the process of burning the scrap tires developed by Gummi-Maier[37] seems to be a satisfactory method of disposal. Successful pyrolysis experiments in an indirectly heated rotary kiln were made by Cobe Steel[38,39]. Similar results will certainly be produced from the Herbold plant[40]. In the Ruhr area a 100 kg/h pilot plant is being built by a consortium of different firms[14] for processing a mixture of used cabling and wiring, scrap tires, and acid resins from the production of phenoplasts. Pyrolysis conditions should be adjusted to give maximum yields of liquid hydrocarbons as well as unsaturated C_5 to C_{10} hydrocarbons and homogeneous depolymerized products. One of the essential demands is the collection of pollutant material at one end of the process. Concerning the solid pyrolysis products, investigations of the conditions and the possibilities of regaining the metal contained in the scrap tires, provided that it is of satisfactory quality, and the regaining of zinc oxide filler are well to the fore at present[41].

Investigations into the utility of the carbon soot separated and into production of an active charcoal-like product are being carried out.

Takamura et al.[42] have shown that the carbon soot produced by pyrolysis of scrap tires can be reused as filler for new tires and also processed into active charcoal.

Gasification in autoclaves[39] and vacuum pyrolysis[43] are also being actively considered, but process development is still at an early stage. All the processes mentioned above use crushed feed which causes considerable expense. Our observations using large pieces of tires for the fluidized bed pyrolysis, would certainly suggest that a suitably dimensioned fluidized sand bed could pyrolyze scrap tires without prior size reduction, with a space-time yield of 1.3 tons.

6. Interim Summary

It is hardly surprising that polymers are pyrolyzed in fluidized sand beds. The relatively high yields of aromatic compounds obtained in very fine sand beds are understandable

in view of the investigations on single plastic particles. While pyrolysis with indirectly heated sand beds excluding oxygen is certainly disadvantageous with regard to the process heat supply, it does afford decomposition products that can be separated in adequate purity at low cost, and which can be reused as chemical raw materials. This could turn out to be economically viable if the price of raw materials for chemical processes remains higher than that of hydrocarbon fuels, or if hydrocarbons relinquish their role as the principal source of energy. To minimize separation costs, and to avoid corrosion damage and pollutant emissions, it would seem appropriate (i) to eliminate hydrolyzable material from a mixture of plastic waste by hydrolysis at temperatures below 200 °C[53–80], (ii) to dehydrochlorinate the residue at 350 °C, and (iii) to pyrolyze the dehydrochlorinated polyenes together with the hydrocarbon-rich polymers at 600 to 800 °C. Catalytically active fluidized beds following the actual pyrolysis reactor would limit and standardize the product spectrum. Studies on this aspect of current research and process data pertaining to the pilot plant described in Section 3 will be published in future paper.

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Dual-Wavelength Spectrophotometry

By Shozo Shibata[*]

At present, dual-wavelength spectrophotometry is probably the least well known of the techniques of absorption spectrophotometry. However, recent improvements in application techniques have shown that for various organic and inorganic materials dual-wavelength spectrophotometry can provide higher sensitivity and selectivity than conventional spectrophotometry. This article reviews the principles and scope of dual-wavelength spectrophotometry, including derivative absorption spectrophotometry, in the hope that these techniques may be adopted more frequently in the future for resolving many analytical problems.

1. Introduction

In 1951 *Chance*[1,2] proposed a new technique, "dual-wavelength spectrophotometry", for the measurement of turbid samples in biochemical analysis, and many important papers based on this technique have since been reported in this special field. Although the dual-wavelength technique is used primarily for the rapid and precise measurement of small absorbance changes at fixed pairs of wavelengths in turbid suspensions, it is also useful for the measurement of transparent solutions. However, this new technique remained unfamiliar in analytical and other branches of general chemistry up to the time of our systematic experiments[3-12]. Perhaps the main reason for this was that "dual-wavelength" was confused with "dual-beam", and that dual-wavelength was erroneously assumed to involve taking absorption measurements at two wavelengths and solving for concentration with simultaneous equations. In addition to this misunderstanding, many chemists were unable to appreciate the essential significance of differential absorbance ΔA. It is hoped that the present review might contribute to dual-wavelength spectrophotometry, including differential absorption spectrophotometry (derivative spectrometry), being fully exploited in the future as a valuable tool for resolving many analytical problems.

2. Principle of the Method

Since the dual-wavelength technique is not yet very familiar in analytical chemistry, we shall first of all describe the principle involved.

In dual-wavelength measurement, light from a highly stabilized tungsten-iodide or deuterium lamp is divided into two beams in two grating monochromators. The light beams of different wavelength from the two gratings are time-shared through a single cell by means of a rotating sector, and the difference ΔA between the absorbances at wavelength λ_1 and λ_2 is measured. Even a very slight change in the absorbance of a sample can thus be determined accurately on using maximum scale expansion. Since only one cell is used in the dual-wavelength method, various errors which are likely to occur in classical spectrophotometry, such as those due to deviations in cell position or cell constant, and to differences between sample and reference solution, such as turbidity and concentration, can be completely eliminated. Namely, dual-wavelength spectrophotometry minimizes the problems of scattering, unequal pathlengths and unequal reagent concentrations by using the sample itself as the reference solution. The principle of the method is shown schematically in Figure 1.

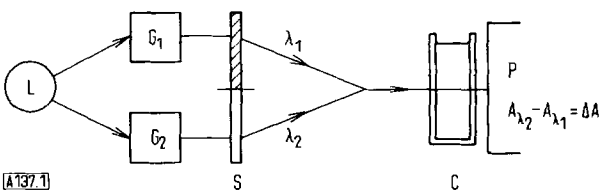

Fig. 1. Principle of dual-wavelength spectrophotometry. L, light source; G_1, G_2, gratings; P, photomultiplier; S, rotating sector; C, cell.

The photosignals are converted into electrical signals by means of a head-on type photomultiplier and are led into the gate circuit through the pre-amplifier. The gate circuit, operated by reference signals synchronized with the chopper, transmits alternate signals in the sequence λ_1 signal, zero signal, λ_2 signal, zero signal, and so on, to the respective hold circuits provided for the λ_1, λ_2, and zero signals. Undesirable influences such as light source fluctuation are automatically eliminated by controlling the voltage applied to the photomultiplier by means of the reference signal (λ_1 signal); the difference between the applied voltage and the reference voltage remains constant at zero signal. The signal-hold circuit feeds back this output to give a correction which makes the pre-amplifier output zero when no photosignal is received. This prevents any spurious signals that may be caused by the dark current of the photomultiplier or stray light. The λ_2 signal is used as the sample signal, and linear recording is made either of transmittance or, through a log converter, of absorbance. By these electrical techniques the peak noise is reduced to 0.0002 of the absorbance. The absorbance scale is therefore expanded one hundred-fold in comparison with conventional spectrophotometers; consequently, the dual-wavelength method is especially useful for measuring very small amounts of samples, and for observing the behavior of substances in very low absorbance ranges.

3. Background of the Principle

Normally, in conventional spectrophotometry the net absorbance A of the sample at fixed wavelength λ is measured by comparison with the reference solution, as shown in Figure 2. If, however, the sample solution contains any other back-

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ground caused by turbidity or interfering components, determination of the component under investigation is no longer possible.

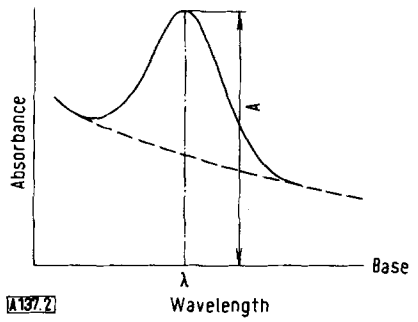

Fig. 2. Measuring absorbance in conventional spectrophotometry.

Actually, the measurement of total absorbance is not absolutely necessary for the quantitative determination of any component or chemical reaction. Hence, in dual-wavelength spectrophotometry, the absorbance difference ΔA between two wavelengths λ_1 and λ_2 is measured as shown in Figure 3, so that no reference solution is required. The most important prerequisite is a linearity or proportionality between measured signals and concentration of the component under investigation. Thus, many types of background can be eliminated by selecting a suitable combination of two wavelengths.

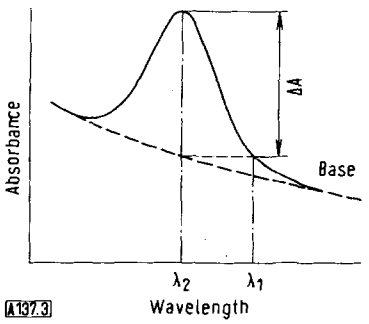

Fig. 3. Measuring absorbance in dual-wavelength spectrophotometry.

In kinetic experiments on the course of a chemical reaction, a wavelength that is not absorbed or an isosbestic point is generally chosen for the "reference beam", and another wavelength that is strongly absorbed by the sample is chosen for the "analytical beam". In this way, the pseudo-absorbance depending on the scattering or any other interfering backgrounds can be cancelled with dual-wavelength measurement; that is, the pseudo-absorbance A_p is detected at λ_1, and the pseudo-absorbance and genuine absorbance A_g are detected at λ_2. The absorbance difference ΔA between λ_1 and λ_2 can then be determined instrumentally.

$$A_{\lambda 2} - A_{\lambda 1} = \Delta A = (A_p + A_g) - A_p = A_g \qquad (1)$$

Quite generally, the special merits of dual-wavelength spectrophotometry are as follows:

1. Extremely small variations in absorbance can be detected[14] in samples having comparatively strong absorbance and pronounced scattering properties. Such small variations can be detected simply by taking the balance between the absorbance values at two different wavelengths λ_1 and λ_2. Hence, the dilutions and filtrations often required for the preparation of samples in conventional spectrophotometry are no longer necessary.

2. Exact measurement of a sample whose absorbance is very weak without having to use a reference solution. Usually the full-scale absorbance is 0.000 to 0.010 or 0.005 for the smallest measurement range.

3. The simultaneous determination of the components of a mixture as well as the masking of components can be carried out very easily.

4. Derivative spectra can be produced by means of wavelength scanning with λ_1 and λ_2 values set close to one another, so that many materials can be determined.

5. If a reference sample is unavailable, a special relative spectrum or genuine absorption spectrum can be obtained by means of wavelength scanning with fixed λ_1.

6. Kinetics of simultaneous reactions in a sample can be monitored with two-pen recorders at λ_1 and λ_2 respectively.

7. All instruments can be used both for the dual-wavelength method as well as for the conventional split-beam method.

4. Chemical Reactions in Turbid Solution

Figure 4 shows the absorption spectra of the oxidized and reduced forms of cytochrome c. In this example, the isosbestic point chosen as the reference wavelength is designated as λ_1. The wavelength chosen for the absorption measurement is designated λ_2, the absorption maximum for the reduced form. Although three other isosbestic points exist, the closest isosbestic point to λ_1 should be chosen so as to guarantee

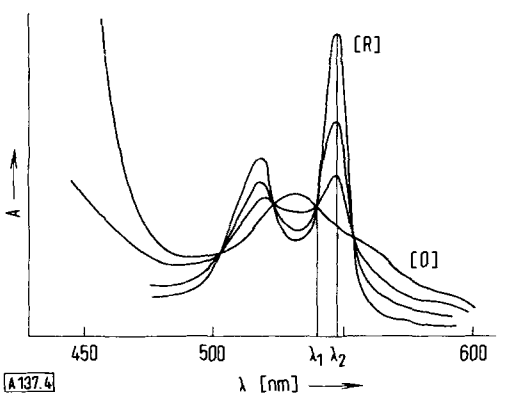

Fig. 4. Absorption spectra of oxidized [O] and reduced [R] cytochrome c.

scattering similarities; this is necessary since scattering, as known for Rayleigh scattering, is wavelength dependent. Thus, we can monitor the degree of reduction of the sample with time. In dual-wavelength spectrophotometry changes in particle size due to swelling or aging are also of little consequence; hence, this method is extremely well suited for the investigation of mitochondria suspensions. Generally, the optical chopper

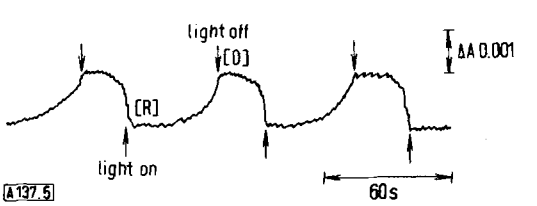

Fig. 5. Photooxidation of cytochrome f.

in commercially available dual-wavelength spectrophotometers operates at 600 to 1000 Hz. Consequently, the measurement of rapid chemical reactions is also possible. Figure 5 shows the photochemical redox reaction of cytochrome f.

5. Analysis of Mixtures

On using the dual-wavelength technique, the simultaneous analysis of multicomponent systems, or masking of the various components, can be carried out very easily and accurately without any calculations.

5.1. Equi-absorption Method

Suppose that a two-component sample contains x and y. The measured absorbances at each wavelength λ_1 and λ_2 are

$$A_{\lambda 1} = \varepsilon_x c_x + \varepsilon_y c_y \quad (2)$$

$$A_{\lambda 2} = \varepsilon_x c_x + \varepsilon'_y c_y \quad (3)$$

where, ε_x and ε_y are the molar absorptivities of the x and y components at λ_1, respectively; ε'_x and ε'_y are the molar absorptivities of the two components at λ_2; c_x and c_y are the concentrations (mol/l) of the components.

Then, the absorbance obtained in the dual-wavelength measurement is

$$A_{\lambda 2} - A_{\lambda 1} = \Delta A = (\varepsilon'_x c_x + \varepsilon'_y c_y) - (\varepsilon_x c_x + \varepsilon_y c_y) \quad (4)$$

If the second component y shows the same absorbance at both wavelengths λ_1 and λ_2, *i.e.* if $A_{y\lambda 2} - A_{y\lambda 1} = 0$, equation (4) simplifies to

$$\Delta A = \varepsilon'_x c_x - \varepsilon_x c_x \quad (5)$$

Since the difference absorbance ΔA is now no longer dependent on the concentration of the component y, it is possible to eliminate the influence due to component y.

5.1.1. Initial Selection of Approximate Values for λ_1 and λ_2

This can be done either by drawing diagrams or by investigating the individual components by wavelength scanning with one wavelength fixed.

Figure 6 shows the absorption spectra of arsenazo I (3-[(2-arsonophenyl)azo]-4,5-dihydroxy-2,7-naphthalenedisulfonic acid) and arsenazoIII (3,6-bis[(2-arsonophenyl)azo]-4,5-dihydroxynaphthalene-2,7-disulfonic acid) in aqueous solution at pH 2.0. As a rule, the synthesis and purification of bisazo compounds is very difficult because the corresponding monoazo compound is also always formed in the reaction. Therefore, the purity must be checked. If the wavelength of maximum absorbance for arsenazo I at 502 nm is chosen as the analytical wavelength, λ_2, a line is drawn vertically from this peak to the *x* axis. A point of intersection is then obtained on the absorption spectrum of arsenazo III, and a line is drawn from this point, parallel to the *x* axis, to another absorption point λ_1. At the combination λ_1, λ_2, the baseline remains unchanged when the concentration of arsenazo III is altered, *i.e.* $A_{\lambda 2} - A_{\lambda 1} = \Delta A = 0$. Accordingly,

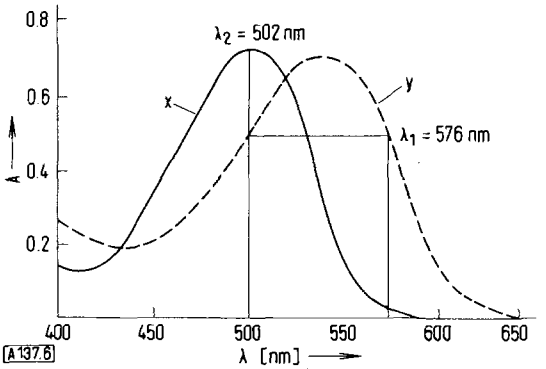

Fig. 6. Selection of λ_1 and λ_2 by drawing figures. pH 2.0, 2.0 mg/100 ml of each component, arsenazo I (x) and arsenazo III (y).

any variation in the concentration of the arsenazo III has no influence on the determination of arsenazo I unless the soluble species is altered as a result of polymerization. Of course, at the selected combination of λ_1 and λ_2, the ΔA value for arsenazo I should be sufficiently large for measurement. For the system shown in Figure 6, the combination 502—567 nm would be selected. Generally, selection of the combination of λ_1 and λ_2 depends on the shape of each spectrum. If the maximum absorbance wavelength cannot be used as the analytical wavelength, any other suitable wavelength in the absorption spectrum can be selected.

Although in the above description, λ_1 and λ_2 are determined for a single concentration of arsenazo III, it is also possible to use several samples having different concentrations. This method then enables any changes in the soluble species, caused by polymerization, dissociation or other chemical or physical effects, to be easily checked from the shape of the spectra. Initially, it is necessary to choose an analytical wavelength from the normal absorption spectrum of arsenazo I; as mentioned above 502 nm was selected. The fixed wavelength λ_2 is then set at 502 nm, and the absorption spectra at various concentrations of arsenazo III are measured with λ_1 as the scanning wavelength. If the soluble species remain unaltered, an isosbestic point can be observed on the baseline, *i.e.* the differential absorbance ΔA between 502 nm and this point is zero. Spectra obtained in this way for arsenazo III are shown in Figure 7.

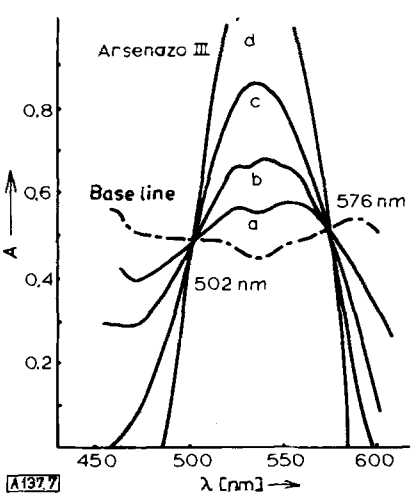

Fig. 7. Selection of λ_1 and λ_2 from absorption spectra with λ_2 fixed (502.0 nm) and λ_1 as the scanning wavelength. Arsenazo III (mg/100 ml): a) 1.0; b) 2.0; c) 4.0; d) 8.0.

5.1.2. Precision Method of Selecting Optimum Wavelength

In this method, the changes in the differential absorbance as a function of variation in concentration, in our example of arsenazo III, are measured 5 or 6 times in the vicinity of the temporary wavelength settings, so that λ_1 and λ_2 can be finally set at wavelengths which minimize changes in the difference of absorbance. The wavelength λ_1 is first altered in one direction or the other by about 1 nm and the direction and size of the change in ΔA observed. Then, both wavelengths are finally adjusted successively until the differential absorbance becomes zero despite variations in the concentration of arsenazo III. The procedure for selecting λ_1 and λ_2 in this way is shown in Figure 8.

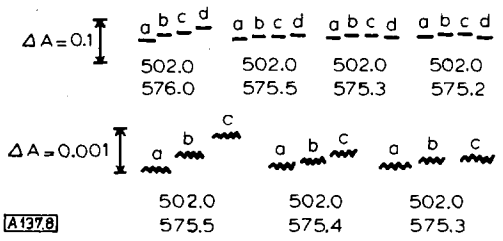

Fig. 8. Precise method for selection of λ_1 and λ_2. Arsenazo III (mg/ml): a) 0.25; b) 0.50; c) 1.00; d) 2.00.

With a scale range of 0.1 absorbance unit, this procedure presents few problems; but great care is needed when the full scale range is 0.01 absorbance unit. In this way a suitable combination for λ_1 and λ_2 of 502.0 and 575.3 nm was established for the determination of arsenazo I in the presence of arsenazo III at pH 2. Optimum selection of λ_1 and λ_2 for the determination of arsenazo III can be accomplished in a similar way. This method enables easy and accurate determination of about 0.5 % of arsenazo I in arsenazo III[7].

5.2. Signal Multiplier Method

When the absorptions of the second component y differ from each other at each of the combinations of two wavelengths, as shown in Figure 9, then the signal multiplier in the instrument is adjusted, so that the second component y does show the same absorbance at wavelengths λ_1 and λ_2, *e.g.*

$$\varepsilon_y c_y = k\varepsilon'_y c_y \tag{6}$$

Then

$$A_{\lambda 2} - A_{\lambda 1} = \Delta A = k(\varepsilon'_x c_x + \varepsilon'_y c_y) - (\varepsilon_x c_x + \varepsilon_y c_y) = k\varepsilon'_x c_x - \varepsilon_x c_x \tag{7}$$

Since the differential absorbance ΔA is independent of the concentration of the component y in Eq. (7), it is possible to determine quantitatively the x component in the mixture. In this technique, two signals for λ_1 and λ_2 are converted into absorbance values by the log-converters, and independently multiplied by means of the function generators. Hence, the differential absorbance ΔA obtainable with this measurement is

$$\Delta A = k_2 A_{\lambda 2} - k_1 A_{\lambda 1} \tag{8}$$

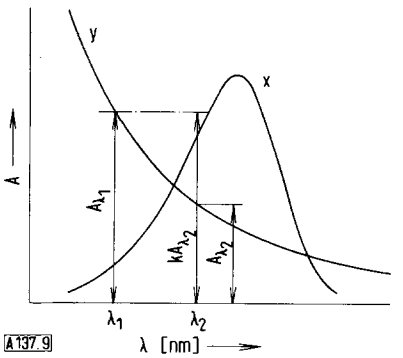

Fig. 9. Principle of signal multiplier method.

5.2.1. Determination of Three-Component Mixtures[24]

If we can choose two wavelengths λ_1 and λ_2 at the intersection of the absorption curves of two components y and z, the x component in the mixture can be determined as follows:

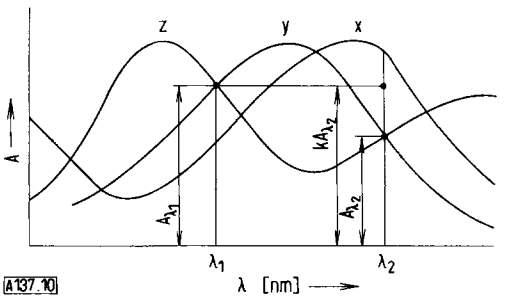

Fig. 10. Analysis of three-component mixtures.

As shown in Figure 10, the absorbance at λ_2 is adjusted to the same value as at λ_1 by the function generator. Then,

$$\varepsilon_y c_y = \varepsilon_z c_z = k\varepsilon'_y c_y = k\varepsilon'_z c_z \tag{9}$$

from which it follows that

$$A_{\lambda 2} - A_{\lambda 1} = \Delta A = k\varepsilon'_x c_x - \varepsilon_x c_x \tag{10}$$

Practical examples demonstrating the successful application of dual-wavelength spectrophotometry to multicomponent systems include the analysis of mixtures of phthalic acid

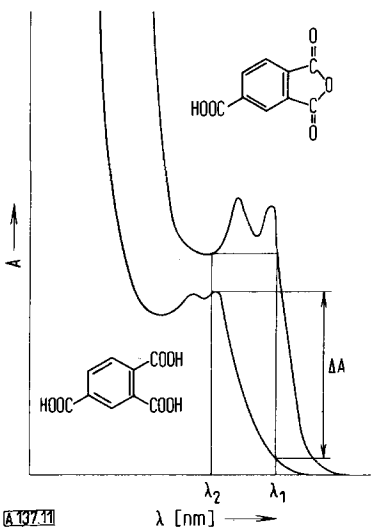

Fig. 11. Determination of trimellitic acid in the presence of its anhydride. $\lambda_1 = 307.6$ nm; $\lambda_2 = 290$ nm.

isomers, of mixtures of food coloring agents, of L-fucose in serum, of the vitamins A and E, polystyrene in durene[22], ephedrine in alkaloids, of amylose[15], and of trimellitic acid and its anhydride (Fig. 11), salicylic acid and 3- and 5-nitrosalicylic acid[21], and of isomeric guaiacol sulfonates in pharmaceutical preparations[13].

6. High-Sensitivity Analysis of Inorganic Substances

Many highly sensitive chromogenic reagents for metals (complexing agents) with molar absorptivities of the order of 10^5 are now known. Therefore, the combination of these reagents with the dual-wavelength technique affords a remarkably sensitive colorimetric method.

6.1. Determination of ppb Amounts of Cobalt with 4-[(3,5-Dichloro-2-pyridyl)azo]-*m*-phenylenediamine[6, 10]

In the conventional method the net absorption of the sample at the wavelength of maximum absorption of the cobalt complex relative to water or reagent blank is measured. In dual-wavelength measurements λ_1 is set to the wavelength for the absorption peak of the complex and λ_2 to the wavelength for the absorption peak of the reagent. Hence, the decrease in the reagent absorption caused by the complex formation is directly additive to the change in absorbance caused by the chelation. Thus the apparent molar absorptivity of the cobalt chelate is increased appreciably (see Fig. 12). By this method, for example, the calibration curve for 1—5 ppb of cobalt is linear through the origin with a slope corresponding to a value for $\Delta A_{570-424\,nm}$ of 0.0028 per ppb of cobalt.

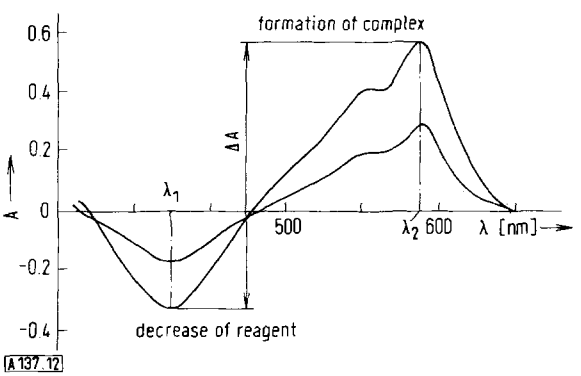

Fig. 12. Differential absorption spectra of 4-[(3,5-dichloro-2-pyridyl)azo]-*m*-phenylenediaminecobalt complexes.

$$\Delta A = A_{\lambda 2} - (-A_{\lambda 1}) = A_{\lambda 2} + A_{\lambda 1}.$$

The dual-wavelength method increases the apparent molar absorptivity of the cobalt-4-[(5-chloro-2-pyridyl)azo]-*m*-phenylenediamine complex ("5-Cl-PADAB"), (Merck) from $1.13 \times 10^5\,l\,mol^{-1}\,cm^{-1}$ to $1.75 \times 10^5\,l\,mol^{-1}\,cm^{-1}$. Generally, the choice of the combination of two wavelengths is unlimited (cf. Fig. 13).

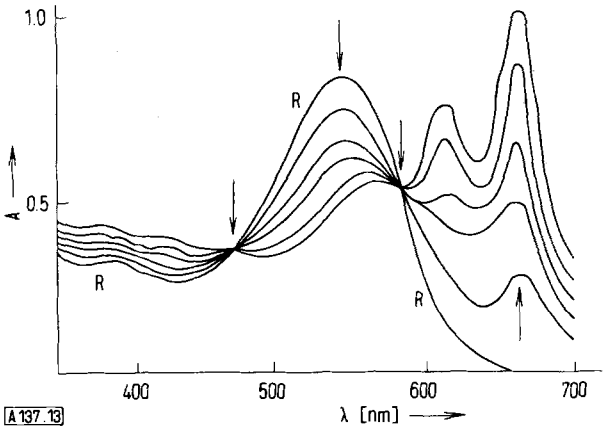

Fig. 13. Absorption spectra of the thorium-arsenazo III complex. 8 N HCl solution, R = Arsenazo III.

6.2. Determination of ppb Amounts of Mercury with Dithizone in Aqueous Solution[27]

Dithizone can be dissolved in aqueous solutions of triton X 100; hence trace amounts of mercury can be determined in an aqueous solution without solvent extraction. The use of large amounts of dithizone can be avoided by using the equi-absorption method (cf. Fig. 14). In this method, the dithizone should be converted into more stable oxidized yellow species by addition of hydrogen peroxide.

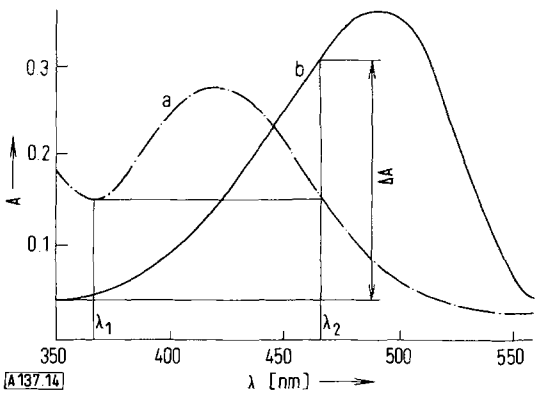

Fig. 14. Determination of mercury with dithizone. $\lambda_1 = 368$ nm, $\lambda_2 = 468$ nm. (a) Dithizone, (b) mercury dithizonate.

The detection limit of the method is 1.8 ppb of mercury and the calibration curve remains linear up to about 40 ppb.

7. Derivative Absorption Spectrometry

The advantages of directly recording a curve of the first or second order differential coefficient of absorbance A or transmission T with respect to wavelength λ, *i.e.* $dA/d\lambda$ or $d^2A/d\lambda^2$, *versus* wavelength, have already been pointed out by *Giese* and *French*[20], and *Saidel*[19]. The first derivative spectrum can be recorded with a conventional double-beam instrument and attachments or with a specially designed derivative spectrophotometer; however, these techniques are rather complicated. Such spectra can be recorded easily by dual-wavelength measurements, if the two wavelengths λ_1 and λ_2 are set very close to each other (usually 1—2 nm), and scanned simultaneously. A further advantage is that these differential spectra can also be recorded electrically.

The merits of directly recording a curve of the first or second order differential coefficient of absorbance or transmission are as follows:

1. Even when two or more absorption bands completely or almost completely overlap, each of the bands can be detected.

2. Very small absorption bands which lie on a steep flank of an absorption curve, and any shoulders in the absorption curves, are clearly resolved.

3. Very broad absorption bands can be located accurately.

4. Generally, the differential coefficient at a specific wavelength is linearly related to the concentration of the corresponding components, thus permitting their determination.

5. Variations in turbidity or background caused by interfering components do not affect measurements, since λ_1 and λ_2 are set close to each other.

It would appear, therefore, that derivative spectrophotometry should facilitate the detection and determination, of, for example, impurities in drugs and chemicals, of food additives, and of industrial wastes. In addition to its use in chemical analyses, this method is also very useful for determination of the fine structure of numerous organic compounds[26].

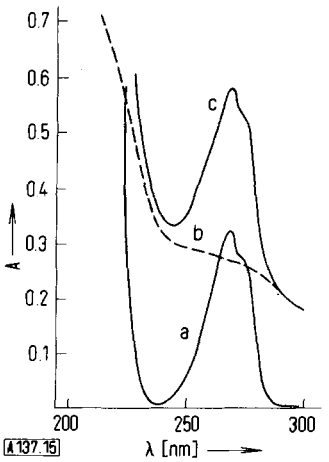

Fig. 15. Absorption spectra of phenol. a) Phenol in aqueous solution; b) turbid industrial waste free from phenol; c) phenol in turbid industrial waste.

Figure 15 shows that the absorption spectrum of phenol in industrial wastes is increased appreciably by the effects of turbid materials, thus making an accurate analysis of phenol in turbid solution very difficult by conventional spectrophotometry. The first derivative spectra of phenol in industrial wastes are shown in Figure 16; here, it can be seen that the distance between the maximum and minimum of the differential coefficient of the absorption band of phenol is constant, *i.e.* the background underlying the absorption band of interest has been eliminated[11].

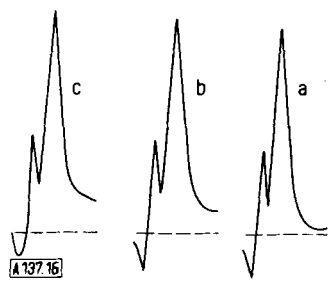

Fig. 16. First-derivative absorption spectra of phenol at various concentrations of turbid materials. Turbidity: a < b < c.

The qualitative and quantitative determination of a mixture of phenols is illustrated in Figure 17[8]. While the components cannot be distinguished in their normal absorption spectra, the derivative spectra clearly show two components, *i.e.* 2,4-dichlorophenol and 2,4,6-trichlorophenol. The second-derivative spectra of two food additives are shown in Figure 18. The influence of New Coccine (C.I. 16255) has been almost eliminated from the spectrum of Phloxine (C.I. 45410).

A second-derivative spectrophotometer for use in the measurement of very small concentrations of certain gases in common air pollutants, such as ammonia, sulfur dioxide, nitrogen mono- and dioxide, ozone, and carbon monoxide, has recently been reported by *Williams* and *Harger*[25].

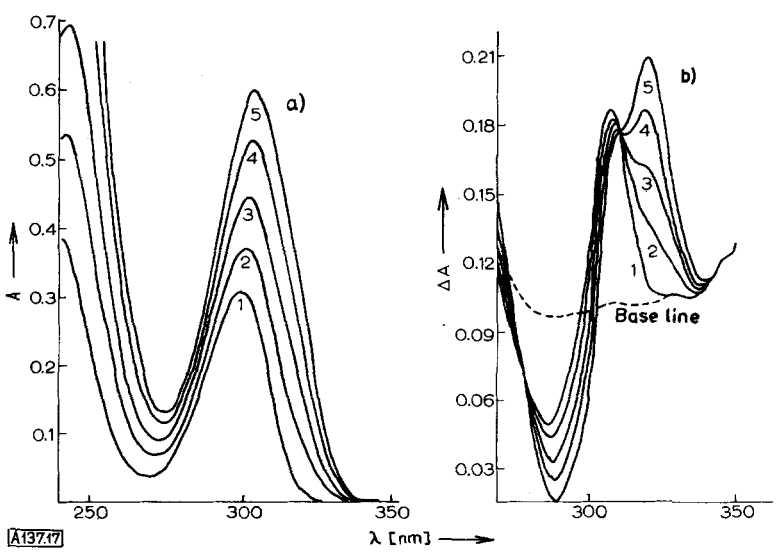

Fig. 17. Analysis of phenol mixtures. a) Absorption spectra; b) derivative spectra ($\Delta\lambda = 2$ nm, $S = 0.25$ mm). 1) 2,4-Dichlorophenol, 10 ppm; 2) (1) plus 5 ppm 2,4,6-trichlorophenol (TCP); 3) (1) plus 10 ppm TCP; 4) (1) plus 15 ppm TCP; 5) (1) plus 20 ppm TCP.

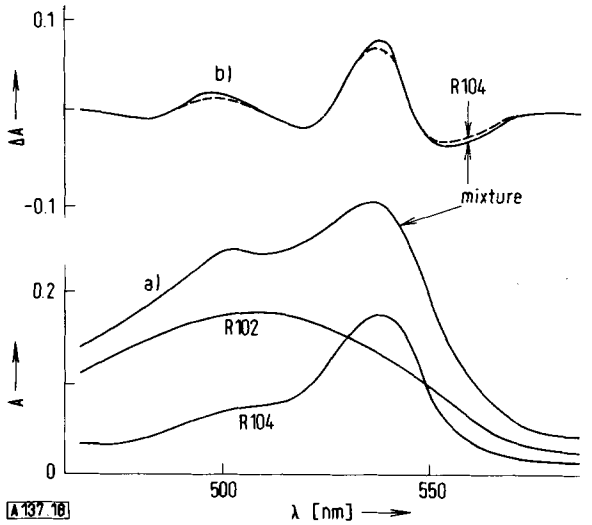

Fig. 18. Second-derivative spectra of food color mixtures. a) Absorption spectra, R 102 (New Coccine, C.I. 16255) and R 104 (Phloxine, C.I. 45410). b) Second-derivative spectra.

8. Densitometry by Means of Dual-Wavelength Measurements[17, 23]

The characteristic features of the dual-wavelength spectrophotometer can be utilized so as to compensate background interference by determining the optical densities at two carefully selected wavelengths. The advantage of this technique is that both the analytical and reference wavelengths pass through exactly the same portion of, *e.g.* a chromatogram[18], thus eliminating any artefacts due to substrate differences.

9. Simultaneous Monitoring of Two Phenomena

If it is desired to monitor the courses of two simultaneous reactions at arbitrary wavelengths λ_1 and λ_2, kinetic measurements can be carried out under identical conditions by utilizing only one cell and a two-pen recorder.

10. Summary

Many other useful applications of dual-wavelength spectrophotometry may be expected, *e.g.* in colloid titrations, photometric titrations in turbid samples, capillary spectrophotometry[12], determination of complex formation constants by ligand exchange reactions, and investigation of various catalytic, fluorescence, or photochemical reactions. At the present time, it is not only useful in analytical chemistry but also in process control in industrial chemistry. For instance, this technique has been applied to quality control of inks, thermopapers, photochromic materials[16], pharmaceutical products, and industrial waste.

Although the dual-wavelength technique is generally simple to use, the measurements on some chemical reactions at small absorbances is appreciably influenced by temperature. Therefore, temperature control of the cell compartment is advisable.

The ability of dual-wavelength spectrophotometry to extend the proven effectiveness of ultraviolet/visible absorption spectrophotometric techniques by overcoming limitations in selectivity and sensitivity has certainly been demonstrated in the field of general analytical spectrophotometry. The following short bibliography is representative and not exhaustive. A comprehensive bibliography may be obtained from our laboratory.

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

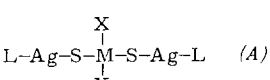
Complexes Having Thiometalate Ions as Bridging Ligands

By *Elisabeth Königer-Ahlborn* and *Achim Müller*[*]

Dedicated to Professor Oskar Glemser on the occasion of his 65th birthday

Unlike oxometalate ions, thiometalate ions can be bonded as bidentate chelate ligands in transition metal complexes such as $[Ni(WS_4)_2]^{2-}$ [1]. No complex has hiterto been reported in which a thiometalate ion acts as a bidentate bridging ligand.

We have now been able to isolate the compounds $[(C_6H_5)_3PAgS]_2MoS_2$ (violet) *(1)*, $[(C_6H_5)_3PAgS]_2MoOS$ (red) *(2)*, $[(C_6H_5)_3PAgS]_2MoO_2$ (orange) *(3)*, $[(C_6H_5)_3PAgS]_2WS_2$ (orange) *(4)*, and $[(C_6H_5)_3PAgS]_2WOS$ (yellow) *(5)* in crystalline form, and to characterize them by elemental analysis, powder diffraction diagrams, and vibrational and electronic absorption spectra.



M = Mo, W; X = O, S; L = $(C_6H_5)_3P$

The vibrational spectra reveal that all compounds of the homologous series possess a trinuclear skeleton corresponding to structure *(A)* (cf. Table 1).

Compared with the weighted average of the frequencies of the MS stretching vibrations of the free ions (*e.g.* MoS_4^{2-}: $\nu_1 = 458$, $\nu_3 = 472\,cm^{-1}$ [2]; $\nu_{av} = 469\,cm^{-1}$) the spectra of the corresponding complexes display bands that are shifted to lower wave numbers and can be assigned to MS bridge vibrations. Coordination of all the chalcogen atoms is ruled out because frequencies of the stretching vibrations of terminal MO or MS groups are observed in the spectra. They are expectedly shifted to higher wave numbers relative to the weighted average of the stretching frequencies of the free ions[2]. We have already drawn analogous conclusions for compounds in which these anions occur as chelate ligands. Confirmatory evidence subsequently came from experimental data for compounds substituted by metal isotopes and from complete crystal structure determinations[3].

Compared with the bands in the electronic absorption spectra of the free ions[1], which correspond to charge transfer transitions, some broadening of these bands is observed in the present compounds.

Powder diffraction patterns show *(1)* and *(4)*, as well as *(2)* and *(5)*, to be isotypic.

Procedure:

A solution of $(NH_4)_2MoS_4$[4] (0.16 g) [or Cs_2MoOS_3 (0.3 g)[5], $(NH_4)_2MoO_2S_2$ (0.14 g)[4], $(NH_4)_2WS_4$ (0.22 g)[6], or Cs_2WOS_3 (0.35 g)[5]] in H_2O (*ca.* 100 ml) is extracted with a solution of $(C_6H_5)_3P$ (0.73 g) and $AgNO_3$ (0.21 g) in CH_2Cl_2 (25 ml). The complex *(1)*, *(2)*, *(3)*, *(4)*, or *(5)* is slowly precipitated from the organic phase by addition of acetone (10 ml) and *n*-pentane (50 ml). (While all the other compounds are obtained pure, soluble impurities must be removed from *(4)* by repeated treatment with CH_2Cl_2.) All the new complexes are only sparingly soluble in organic solvents such as CH_2Cl_2, acetone, and nitromethane.

Table 1. Stretching vibrations (principal bands) [a] in the vibrational spectra of the complexes *(1)* to *(5)* (in cm^{-1}).

Complex		ν(MO)	$\nu(MS)_t$	$\nu(MS)_{br}$	ν(AgS)
$[(C_6H_5)_3PAgS]_2MoS_2$ *(1)*	IR	—	515 [a]	453 (s) 438 (s)	257 (w)
$[(C_6H_5)_3PAgS]_2MoOS$ *(2)*	R	930 (w)	520 (w)	444 (m) 426 (s)	257 (m)
$[(C_6H_5)_3PAgS]_2MoO_2$ *(3)*	IR	921 (s) 884 (s)		445 (m) 429 (s)	257 (w)
$[(C_6H_5)_3PAgS]_2WS_2$ *(4)*	R	—	523 (w) 511 (s)	446 (s) 424 (m)	258 (m)
$[(C_6H_5)_3PAgS]_2WOS$ *(5)*	R	945 (m)	521 (w)	446 (s) 427 (m)	264 (m) 257 (m)

[a] Since $\nu(MS)_t$ is masked in the IR spectrum by a strong band of the $(C_6H_5)_3P$ group, the Raman frequencies are given in those cases where the Raman spectrum could be measured.

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(1), 60537-80-6; *(2)*, 60563-07-7; *(3)*, 60537-81-7; *(4)*, 60537-82-8; *(5)*, 60537-83-9; $(NH_4)_2MoS_4$, 15060-55-6; Cs_2MoOS_3, 14348-14-2; $(NH_4)_2MoO_2S_2$, 16150-60-0; $(NH_4)_2WS_4$, 13862-78-7; $CsWOS_3$, 14348-13-1

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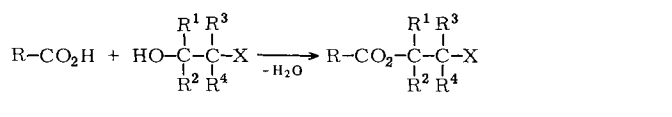
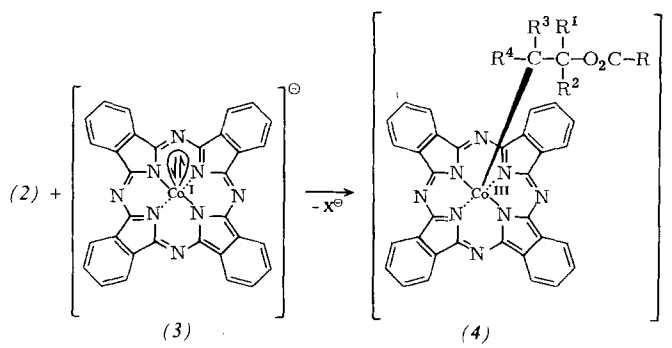
A New Technique of Protecting Groups—Cleavage of β-Halogenated Alkyl Esters with Supernucleophilic Cobalt(I)-phthalocyanine[1]

By *Heiner Eckert* and *Ivar Ugi*[*]

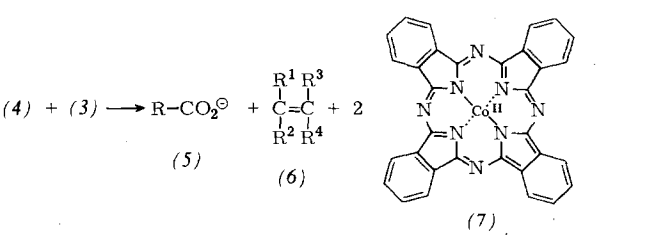
Carboxy groups of α-amino acids and peptides can be protected by esterification with β-halogenated alcohols *(1)* at the C terminus[2]. β-Halogenated alcohols of potential utility are 2-chloroethanol *(1a)* and 2-bromoethanol *(1b)*, 2,2-dibromopropanol *(1c)*, 2,2,2-trichloroethanol *(1d)*, and 2,2,2-trichloro-*tert*-butanol *(1e)* (chloretone).



(1) *(2)*



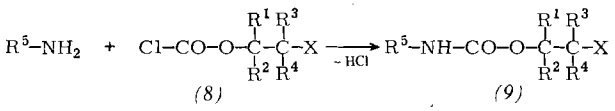
(3) *(4)*



(5) *(6)* *(7)*

$R^1 = R^2 = H, CH_3$; $R^3 = H, CH_3, Cl$; $R^4 = H, X$; $X = Br, Cl$

Amino groups can be provided with urethane protecting groups by reaction with the chloroformates *(8)* of the above alcohols.



(8) *(9)*

Apart from the base-sensitivity of the derivatives of *(1d)*, the lability of urethanes derived from *(1a)* and *(1b)* in alkali hydroxide solution, and the ease of reductive cleavage of the C—X bonds, the protecting groups mentioned are inert towards the deblocking reagents commonly used in peptide chemistry.

We have now found that β-halogenated alkyl esters and urethanes can be cleaved by cobalt(I)-phthalocyanine *(3)*[3] with Li^+ or Na^+ as counterion in methanol, acetonitrile, or acetone at 0 to 20°C. Preliminary experiments had shown that *(3)* is superior to cobaloxime(I)[4] for various reasons.

Cleavage generally proceeds in 60 to 98% yield at a rate that is determined primarily by the constitution of the β-haloalkyl group (see Tables 1 and 2). The reaction is usually three- to ten times slower when performed in acetonitrile and acetone.

Table 1. Reaction times for complete removal of N terminal 2-haloalkoxycarbonyl protecting groups from the urethanes *(9)* with *(3)* in 0.1 M solution at 20°C and the yields of isolated amine component obtained.

N terminal protecting group	Reaction time in methanol	acetone	Yield of amine component [%]
$Cl—CH_2—CH_2—O_2C—$	40 h	—	83 [a]
$Br—CH_2—CH_2—O_2C—$	30—90 min	20 h	70—89 [b]
$H_3C—CBr_2—CH_2—O_2C—$	< 1 min	3 min	77 [c]
$Cl_3C—CH_2—O_2C—$	< 1 min	5 min	91 [c]

[a] Aniline.
[b] Aniline (70—86), amino ester (76—89), dipeptide ester (82), tripeptide ester (80).
[c] Amino ester.

Table 2. Reaction times for complete removal of C terminal 2-haloalkyl protecting groups from the esters *(2)* with *(3)* in 0.1 M solution at 20°C and the yields of isolated acid component obtained.

C terminal protecting group	Reaction time in methanol	aceto-nitrile	acetone	Yield of acid component [%]
$Cl—CH_2—CH_2—$	50 h	—	—	66 [a]
$Br—CH_2—CH_2—$	30—50 min	—	4 h	57—85 [b]
$H_3C—CBr_2—CH_2—$	—	< 1 min	—	95 [a]
$Cl_3C—CH_2—$	< 1 min	—	1 min	98 [a]
$Cl_3C—(CH_3)_2C—$	—	< 1 min	—	92 [a]

[a] Benzoic acid.
[b] Benzoic acid (77), *N*-acyl amino acid (57), *N*-acyl dipeptide (85), *N*-acyl tripeptide.

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(1a), 107-07-3; *(1b)*, 540-51-2; *(1c)*, 59992-05-1; *(1d)*, 115-20-8; *(1e)*, 57-15-8; *(2a)*, 939-55-9; *(2b)*, 939-54-8; *(2c)*, 59992-06-2; *(2d)*, 37934-99-9; *(2e)*, 59992-07-3; *(3)*, 18974-06-6; *(8a)*, 627-11-2; *(8b)*, 4801-27-8; *(8c)*, 59992-08-4; *(8d)*, 17341-93-4; *(9a)*, 3747-48-6; *(9b)*, 32353-12-1; $C_6H_5NH_2$, 62-53-3; $C_6H_5CO_2H$, 65-85-0

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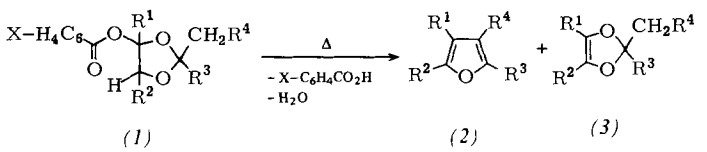
Synthesis of Furan Derivatives from 4-Benzoyloxy-1,3-dioxolane Derivatives

By *Hans-Dieter Scharf* and *Erich Wolters*[*]

Pyrolysis of the readily accessible 4-benzoyloxy-1,3-dioxolane derivatives *(1)*[1] affords, *via* elimination of benzoic acid and water, the furan derivatives *(2)* and small amounts (5 to 10%) of the 1,3-dioxole derivatives *(3)*. The reaction is catalyzed by acids.



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

At 230°C furan yields of 70—90% are obtained when X = *o*-CH_3. At 400°C and 10^{-3} torr the 1,3-dioxole derivatives *(3)* are obtained in 30 to 35 yield. No furans are formed under these conditions.

Under pyrolysis conditions the 1,3-dioxole derivatives *(3)* undergo proton-catalyzed rearrangement to the furan derivatives *(2)*, so that with suitable control of the pyrolysis their formation can be completely suppressed in favor of the furans.

Thus, 2,2-dimethyl-4-methylene-1,3-dioxolane *(4)* as well as 2,2-dimethyl-4-methyl-1,3-dioxole *(6)* rearrange under these conditions to the 2,4-dimethylfuran *(7)*. This suggests the reaction sequence is initiated by 1,3-dioxolan-4-ylium ion *(5)*[2].

Compared to the Paal-Knorr synthesis the reaction described here has the advantage of easy accessibility of starting compounds and compared to the Feist-Benary synthesis the advantage of free choice of substituents in position 3.

General Procedure

Synthesis of the 4-benzoyloxy-1,3-dioxolane derivatives *(1)*:

A mixture of 1,3-dioxolane (1.0 mol) and CuBr (0.5 g) in anhydrous benzene (500 ml) is heated to boiling under nitrogen. *tert*-Butyl peroxybenzoate (0.8 mol) is added dropwise to the stirred mixture over a period of 2—2.5 hours. The CuBr goes into solution with deep blue coloration. The mixture is heated for a further 16 hours then extracted with Na_2CO_3 solution. The aqueous phase is washed several times with ether and the combined organic phases dried over Na_2SO_4. After removal of solvent in a rotary evaporator, the residue is distilled under vacuum in a molecular distillation apparatus.

Pyrolysis of the 4-benzoyloxy-1,3-dioxolane derivatives *(1)*:

Compound *(1)* (0.5 mol) is introduced dropwise over a period of 1.5 h into a flask heated to 230°C and containing a small amount of molten *o*-toluic acid which is stirred with a magnetic stirrer. The furan *(2)* that is formed is slowly distilled off together with water over a 30 cm Vigreux column at normal pressure or under vacuum depending upon the derivative concerned. The distillate is washed with Na_2CO_3 solution, dried, and distilled.

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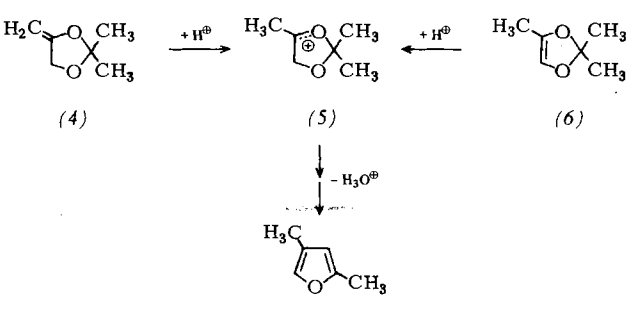
CAS Registry numbers:
(1a), 59953-77-4; *(1b)*, 59953-78-5; *(1c)*, 59953-79-6; *(1d)*, 59953-80-9; *Z-(1e)*, 59953-81-0; *E-(1e)*, 59953-82-1; *(2a)*, 534-22-5; *(2b)*, 59953-83-2; *(2c)*, 59953-84-3; *(2d)*, 42768-88-7; *(2e)*, 625-86-5; *(3a)*, 22945-10-4; *(3b)*, 59983-85-4; *(3c)*, 59953-86-5; *(3d)*, 59953-87-6; *(3e)*, 51494-95-2; *o*-toluic acid, 118-90-1; *tert*-butyl peroxybenzoate, 614-45-9

[1] *O. J. Rawlinson* and *G. Sosnovsky*, Synthesis *1972*, 1.
[2] 1,3-Dioxolan-4-ylium ions like *(5)* have been postulated already by *Meerwein* [3] and *Barton* [4] under different reaction conditions. The formation of furan derivatives has not been observed.
[3] *H. Meerwein, H. Allendörfer, P. Peekmann, Fr. Kunert, H. Morschel, F. Pawellek*, and *Kl. Wunderlich*, Angew. Chem. *70*, 211 (1958).
[4] *D. H. R. Barton, P. D. Magnus, G. Smith, G. Streckert*, and *D. Zurr*, J. Chem. Soc. Perkin Trans. 1, *1972*, 542.

Table 1. Yields and physical data of compounds *(1)* and *(2)*.

	Yield [%]	B.p. [°C/torr]	n_D^{20}	R^1	R^2	R^3	R^4		Yield [%]	B.p. [°C]	$n_D^{Temp.}$
(1a)	63	$66/10^{-2}$	1.5068	H	H	CH_3	H	*(2a)* [b]	80	63	$1.4321^{19.5}$
(1b)	58	$86/7\times10^{-3}$	1.5033	H	H	C_2H_5	CH_3	*(2b)* [b]	80	115	1.4450^{20}
(1c)	49	$97/10^{-2}$	1.5219	H	H	—$(CH_2)_3$—		*(2c)* [b]	77	140	1.4924^{21}
(1d)	50	$105/5\times10^{-3}$	1.5248	H	H	—$(CH_2)_4$—		*(2d)* [b]	72	163.5	1.4944^{21}
(1e) [a]	30	$72/7\times10^{-3}$	1.4992	H	CH_3	CH_3	H	*(2e)* [b]	75	93	1.4413^{20}

[a] Mixture of *Z* and *E* products.
[b] The structure of the furan derivatives was confirmed by comparison with authentic material or by spectroscopic findings and elemental analysis.



(4) *(5)* *(6)* *(7)*

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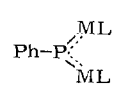
Phosphinidene Complexes as π Ligands[**]

By *Gottfried Huttner, Gerhard Mohr*, and *Albin Frank*[*]

Phenylphosphinidene Ph—P can be stabilized as a bridging ligand in dinuclear transition metal complexes of type *(1)*[1].

In such compounds the octet vacancy at the phosphorus is filled by back bonding from the occupied d orbitals of



(1)

ML = $Mn(CO)_2C_5H_5$

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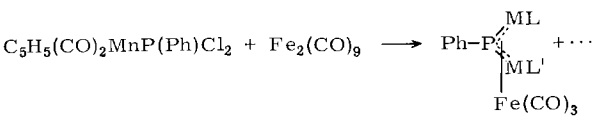
the metal. The trigonal-planar coordination of phosphorus and the properties of the phosphinidene complexes *(1)* suggest description of the bonding in the M═P═M group in terms of the model of a three-center 4π electron system[1,2].

We have now found further evidence substantiating the correctness of this model concept: On attempted dehalogenation of the dichlorophosphane complex $C_5H_5(CO)_2MnP(Ph)Cl_2$ with $Fe_2(CO)_9$ we observed formation of a compound of the novel type *(2)*.



$C_5H_5(CO)_2MnP(Ph)Cl_2 + Fe_2(CO)_9 \longrightarrow$ Ph–P(ML)(ML')–Fe(CO)$_3$ + ···

ML = $Mn(CO)_2C_5H_5$, ML' = $Fe(CO)_4$ *(2)*

The dinuclear phosphinidene complex $C_5H_5(CO)_2Mn{=}P(Ph){=}Fe(CO)_4$ expected as the primary product of dehalogenation could not be detected; instead, the "trinuclear" complex *(2)* is formed in which the three-center 4π system Mn═P═Fe is coordinated as a π ligand to a $Fe(CO)_3$ group (Fig. 1)[3].

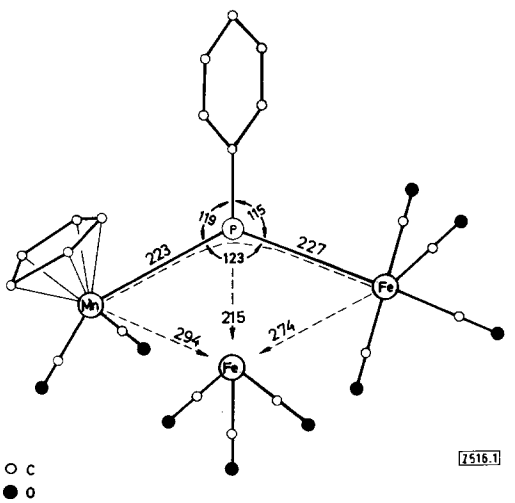


Fig. 1. Molecular structure of the complex *(2)*; distances [pm] and angles [°].

X-Ray structure analysis shows that *(2)* is not a phosphido cluster containing tetracoordinated phosphorus[4,5]: the manganese atom is coplanar with the phosphorus atom, the phenyl carbon atom, and the iron atom of the $Fe(CO)_4$ group (maximum deviation 17 pm). Thus the coordination of the phosphorus in *(2)* corresponds to the trigonal-planar environment observed for the phosphorus atom in dinuclear phosphinidene complexes of type *(1)*. The metal-metal bonds in *(2)* are relatively long[6] and reflect the unusual bonding characterizing this complex, in which the manganese atom and the iron atom of the $Fe(CO)_4$ act as the terminal atoms of a three-center 4π ligand system.

Procedure:

All operations are performed in solvent freed from oxygen and water and under N_2.

$Fe_2(CO)_9$ (1.28 g, 3.52 mmol) is suspended in a solution of $C_5H_5(CO)_2MnP(Ph)Cl_2$ (1.08 g, 3.05 mmol) in toluene (40 ml) and the mixture stirred for 48 h at 40 °C. Filtration from the brown precipitate affords a red solution which is concentrated with silica gel (3 g) at 20 °C until the silica gel appears dry. The silica gel loaded with reaction product is applied at 10 °C to a chromatography column (16 × 2.5 cm; *n*-pentane; silica gel, Merck, 0.063 to 0.200 mm). With pentane/toluene (5:1) a red and a yellowish brown zone are eluted, which both contain very little substance. With pentane/toluene (2:1) there follows a green zone from which deep green crystals of analytically pure *(2)* can be isolated by removal of the solvent and recrystallization from hexane. Further elution with pentane/toluene (1:1) gives a deep red zone of $C_5H_5MnFe_2PPh(CO)_8$[7]. *(2)* is readily soluble in hexane or toluene and is air-stable in the solid state; m.p. 178 °C (dec.); yield: 100 mg (6 %).

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CAS Registry numbers:
$Fe_2(CO)_9$, 15321-51-4; $C_5H_5(CO)_2MnP(Ph)Cl_2$, 12276-83-4; *(2)*, 60349-47-5

[1] *G. Huttner, H.-D. Müller, A. Frank*, and *H. Lorenz*, Angew. Chem. *87*, 714 (1975); Angew. Chem. Int. Ed. Engl. *14*, 705 (1975).

[2] *G. Huttner, J. v. Seyerl, M. Marsili*, and *H.-G. Schmid*, Angew. Chem. *87*, 455 (1975); Angew. Chem. Int. Ed. Engl. *14*, 434 (1975).

[3] There is an analogy with the π bonding of the three-center 4π electron system Fe═C(R)═OR' of a carbene complex to a $Fe(CO)_3$ group: *G. Huttner* and *D. Regler*, Chem. Ber. *105*, 2726 (1972); *E. O. Fischer, E. Winkler, G. Huttner*, and *D. Regler*, Angew. Chem. *84*, 214 (1972); Angew. Chem. Int. Ed. Engl. *11*, 238 (1972).

[4] *L. Marko* and *B. Marko*, Inorg. Chim. Acta *14*, 239 (1975); *R. C. Ryan* and *L. F. Dahl*, J. Am. Chem. Soc. *97*, 6904 (1975).

[5] 1135 independent, non-zero data (Syntex-P21); solution: Syntex-XTL, $R_1 = 0.058$.

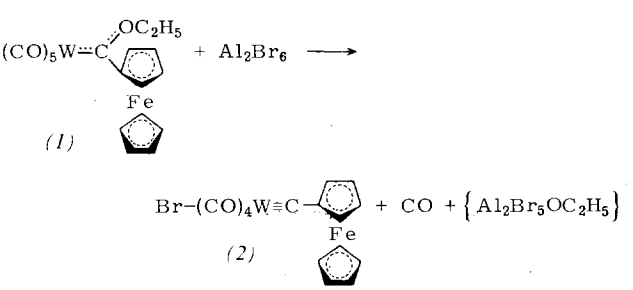
[6] Cf. *E. W. Abel* and *F. G. A. Stone*, Quart. Rev. Chem. Soc. *1970*, 325.—Fe—Fe distances of 265 pm appear to be typical for singly bridged carbonyl-iron complexes: *R. E. Davies*, Chem. Commun. *1968*, 248; *O. S. Mills* and *A. D. Redhouse*, *ibid.* *1968*, 444. The Fe—Mn bonds in $(CO)_4Fe[Mn(CO)_5]_2$ were found to have lengths of 280 and 283 pm: *R. A. Agron, R. D. Ellison*, and *H. A. Levy*, Acta Crystallogr. *23*, 1079 (1967).

[7] *G. Huttner, A. Frank*, and *G. Mohr*, Z. Naturforsch. *31b*, (1976), in press.

trans-Bromo(tetracarbonyl)ferrocenylcarbynetungsten[1]

By *Ernst Otto Fischer, Monika Schluge*, and *Jürgen Otto Besenhard*[*]

On reaction of pentacarbonylethoxy(ferrocenyl)carbenetungsten(0) *(1)*[2] with aluminum bromide at low temperature we obtained crystalline, raspberry-red *trans*-bromo(tetracarbonyl)ferrocenylcarbynetungsten *(2)*. The diamagnetic complex, which is only sparingly soluble in hexane yet readily soluble in polar solvents such as CH_2Cl_2 and acetone, is stable at room temperature for several hours in the solid state even when exposed to the air; in solution slow decomposition takes place above −10 °C.



$(CO)_5W{=}C(OC_2H_5)$–Fe + Al_2Br_6 ⟶ *(1)*

Br–$(CO)_4W{=}C$–Fe *(2)* + CO + $\{Al_2Br_5OC_2H_5\}$

The IR spectrum of *(2)* (in CH_2Cl_2) shows a strong band (E) at 2020 cm^{-1} and a weak band (A_1) at 2112 cm^{-1} in the ν_{CO} region.—In the ^{1}H-NMR spectrum ([D_6]-acetone solution at −30 °C; rel. TMS int.) three signals appear at

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$\delta = 4.58$ (S,5) [C_5H_5], 4.60 (M,2), and 5.00 ppm (M,2) [C_5H_4].—The ^{13}C-NMR spectrum (CD_2Cl_2 solution at -30°C; rel. $CD_2Cl_2 = 54.2$ ppm) shows six signals at $\delta = 275.1$ ($C_{carbyne}$), 193.4 (CO), 89.5, 72.7, 71.6, and 71.0 ppm ($C_{10}H_9Fe$)[3].

The mass spectrum of *(2)* contains the molecular ion at $m/e = 572$ (referred to ^{184}W, ^{56}Fe, and ^{79}Br; ion source TO4, 50 eV).

The reversibility of the oxidation of *(2)* was proven by cyclic voltammetry in 0.5 M KPF_6/DME (1,2-dimethoxyethane; -20°C). The difference between the anodic and cathodic peak potential confirms that a reversible one-electron transfer is involved, as in the case of ferrocene (FcH). Since the electrochemical oxidation of $X(CO)_4W{\equiv}C{-}C{\equiv}CPh$ (X = Cl, Br, I) only takes place irreversibly and does not begin below the range $+1.5$ to $+1.8$ V *vs.* SCE[4] we attribute the reversible oxidation of *(2)* to formation of the carbyne-substituted ferrocenium ion $(2)^+$. There is no indication of a secondary reaction of $(2)^+$—the quotient of the cathodic and anodic peak currents iP_c/iP_a is almost unity, irrespective of the rate of polarization v. Owing to the withdrawal of electrons from the Fc system by the complex carbynetungsten group, $E_{1/2}$ *(2)*/$(2)^+$ is shifted about $+280$ mV *vs.* $E_{1/2}$FcH/FcH$^+$; the ratio iP_a(FcH)/iP_a *(2)* yields a diffusion coefficient for *(2)* which is smaller than that for ferrocene by a factor of about 2.

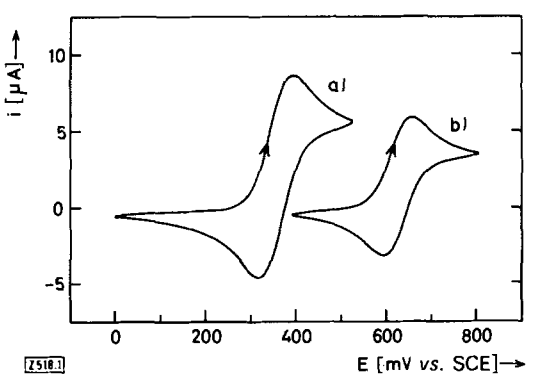

Fig. 1. Cyclovoltammogram of a) ferrocene, and b) *(2)* at Pt. $c = 2 \times 10^{-3}$ mol·l^{-1}; $v = 100$ mV·s^{-1}.

A linear relationship between $E_{1/2}$XFc/XFc$^+$ and the Hammett constants σ_m and σ_p of the substituents X has been demonstrated on many occasions for substituted ferrocenes (XFc)[5]. From the correlation curves determined by *Hoh, McEwen,* and *Kleinberg*[5], values of $\sigma_m = +0.45$ and $\sigma_p = +0.59$ were calculated for $X{=}C{\equiv}W(CO)_4Br$. These values approximate those for $X{=}C{\equiv}N$ ($\sigma_m = +0.56$; $\sigma_p = +0.66$) and thus confirm, in accord with other data, the "electron attracting" influence of the carbyne group.

Experimental:

All operations are carried out in anhydrous, oxygen-free solvents in an inert atmosphere (N_2).

Al_2Br_6 (0.79 g, 1.5 mmol) is added spatula-wise at -78°C to a solution of *(1)* (1.132 g, 2 mmol) in CH_2Cl_2 (70 ml). The solution, which changes color from red-black to deep-blue, is then warmed until gentle evolution of gas occurs. Meanwhile the solution turns raspberry-red in color. It is now stirred for 40 min at -15°C. Adducts of the carbyne complex with Al_2Br_6 are destroyed by addition of about 10 ml methanol. The product is purified by column chromatography on silica gel at -30°C. Dark-red, unreacted *(1)* is first eluted (with CH_2Cl_2/pentane, 1:1). The second, raspberry-red zone is eluted with pure CH_2Cl_2, the eluate evaporated to dryness, and the resulting residue washed three times with pentane at -78°C: cryptocrystalline product; decomposes above 70°C; yield 0.80 g (70 %).

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CAS Registry numbers:
(1), 34691-66-2; *(2)*, 60364-07-0; Al_2Br_6, 18898-34-5; ^{13}C, 14762-74-4

[1] Transition Metal-Carbyne Complexes, Part 22.—Part 21: *E. O. Fischer, E. W. Meineke,* and *F. R. Kreissl,* Chem. Ber., in press.
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[3] Measurements by Dr. *F. R. Kreissl,* TU München.
[4] *H. J. Kalder* and *T. Würminghausen,* private communication.
[5] *G. L. K. Hoh, W. E. McEwen,* and *J. Kleinberg,* J. Am. Chem. Soc. *83*, 3949 (1961); *J. Tirouflet, E. Laviron, R. Dabard,* and *J. Komenda,* Bull. Soc. Chim. Fr. *1963*, 857.

Carbene-Analogous Germylene Complexes[**]

By *Peter Jutzi* and *Wolfgang Steiner*[*]

Using an oxygen-germanium-ylide complex as starting material we have been able to prepare the first true germylene complexes. Thus, reaction of pentacarbonyl[dichloro(tetrahydrofuran)germylene]chromium(0) [compound *(1)*][1] with trimethyl(mesitylthio)silane *(2a)* or trimethyl(methylthio)silane *(2b)* leads, *via* loss of trimethylchlorosilane and tetrahydrofuran, to [bis(mesitylthio)germylene]pentacarbonylchromium(0) [compound *(3a)*] and [bis(methylthio)germylene]-pentacarbonylchromium(0) [compound *(3b)*], respectively.

$$(CO)_5Cr{\leftarrow}\underset{\uparrow}{Ge}Cl_2 + 2\ RSSi(CH_3)_3 \xrightarrow[THF]{} \underset{(1)}{\quad} \qquad \underset{(2)}{\quad}$$

$$(CO)_5Cr{\leftarrow}Ge(SR)_2 + THF + 2\ (CH_3)_3SiCl \qquad (3)$$

(a): R = 2,4,6-trimethylphenyl ; *(b)*: R = CH_3

The complexes *(3a)* and *(3b)* are stable toward atmospheric oxygen but somewhat sensitive toward hydrolysis. They precipitate as orange yellow cubic crystals [*(3a)*, decomp. pt. 141 °C] and yellow-green needles [*(3b)* decomp. pt. 112 °C], respectively, and are very soluble in chlorinated hydrocarbons, carbon disulfide, and benzene, but only moderately soluble in hydrocarbons. The structures have been confirmed by spectroscopic and analytical data and, in the case of *(3a)*, by an X-ray structure analysis[2]. Mass spectra and molecular weight determinations (cryoscopically in benzene) confirm the monomeric structure of the compounds. In the IR spectra (in CH_2Cl_2) three absorptions which correspond to local C_{4v} symmetry are observed in the region of the νCO vibrations [*(3a)*: 2060 (s,A_1), 1990 (m,A_1), 1955 (s,E) cm^{-1}; *(3b)*: 2050 (s,A_1), 1990 (m,A_1), 1945 (s,E) cm^{-1}]. The position of the long-wave A_1 vibration is indicative of the $Ge(SR)_2$ ligands being good π-acceptors. The synthesis of pentacarbonyl(dichlorogermylene)chromium(0) [compound *(4)*] by cleavage of

$$(3a) + 2/3\ BCl_3 \longrightarrow (CO)_5Cr{\leftarrow}GeCl_2 + 2/3\ B(SR)_3 \qquad (4)$$

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THF from *(1)* is not possible[1]. We have succeeded in preparing this complex, however, by reaction of *(3a)* with boron trichloride.

Compound *(4)* precipitates as bright red, needle-like crystals, (decomp. pt. 105 °C), has solubility properties comparable to those of *(3a)* and *(3b)*, but, unlike the latter two compounds, is extremely sensitive toward air and moisture. Its structure was also confirmed by spectroscopic and analytical data. Molecular weight determinations and the mass spectrum are consistent with the monomeric structure of the complex. IR spectrum: νCO (in CH_2Cl_2): 2075 (s,A_1), 1985 (m,A_1), 1960 (s,E) cm^{-1}; νGe—Cl (in Nujol): 360 (w), 320 (w) cm^{-1}. The germylene complexes *(3a)*, *(3b)*, and *(4)* can be readily converted into the corresponding ylide complexes by addition of bases (ether, tertiary amines, or tertiary phosphanes).

Experimental

Preparation of *(3a)* and *(3b)*: 20 mmol of *(2)* or *(3)* [4.48 g *(2)*; 2.40 g *(3)*] is added dropwise to a solution of *(1)* (10 mmol, 2.04 g) in benzene (30 ml) and the mixture is stirred for 30 min at 50 °C. After removal of volatile components the remaining oil is extracted with petroleum ether (boiling range 50—70 °C). On concentration of the extract *(3a)* and *(3b)*, respectively, crystallize out. Recrystallization from petroleum ether affords the analytically pure complexes. Yields: 4.50 g (79 %) *(3a)*; 0.7 g (19 %) *(3b)*.

Preparation of *(4)*: A solution of *(3a)* (10 mmol, 5.67 g) in 100 ml petroleum ether (boiling range 50 to 70 °C) is added to a solution of BCl_3 (6.8 mmol, 0.80 g) in 50 ml petroleum ether at −30 °C. An orange-yellow precipitate of *(4)* immediately separates out and is filtered after 30 minutes' stirring at 0 °C. Recrystallization from petroleum ether affords analytically pure *(4)*. Yield 1.25 g (37 %).

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CAS Registry numbers:
(1), 60260-16-4; *(2a)*, 60253-72-7; *(2b)*, 3908-55-2; *(3a)*, 60260-11-9; *(3b)*, 60260-12-0; *(4)*, 60260-13-1; BCl_3, 10294-35-5

[1] *P. Jutzi* and *W. Steiner*, Chem. Ber. *109*, 3473 (1976).
[2] *G. Huttner*, unpublished work.

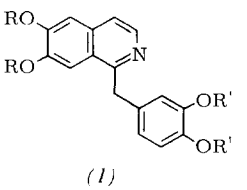
Papaverine Crown Ethers[**]

By *Fritz Vögtle* and *Klaus Frensch*[*]

The endohydrophilic/exolipophilic structure of the crown ethers permits lipophilization of alkali metal ions. As synthetic analogs of the well-known ionophores, neutral ligands of the crown ether type have contributed greatly to our understanding of selective ion transport processes in biological membranes.

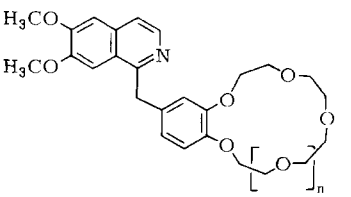
The present communication concerns the novel concept of altering the hydrophilic/lipophilic properties of physiologically active molecules by intramolecular incorporation of crown ether rings and especially of enabling or facilitating selective complex formation with alkali or alkaline-earth metal ions. Thereby it ought to be possible to modify the physiological action, *e.g.* as regards rate and site of attack. The isoquinoline alkaloid papaverine *(1a)*, that constitutes about 0.5 to 1.0 % of opium and is used as an antispasmodic, *e.g.* for relieving spasms of the gastro-intestinal and the bile duct, was considered the best candidate for initial model experiments on account of the two catechol partial structures already present.

We were able to prepare the crown-ether type bridged analog of benzo[15]crown-5[1], papaverine derivative *(2)* (m.p. 104 °C), in 25 % yield by reaction of the doubly demethylated papaverine *(1b)*[2] with 1,11-dichloro-3,6,9-trioxaundecane without employing the dilution principle[3].



(1)

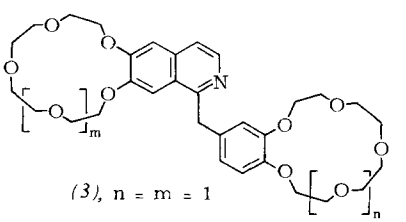
(a): R = R' = CH_3
(b): R = CH_3, R' = H
(c): R = R' = H



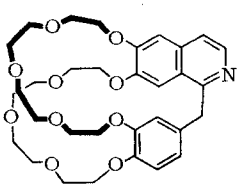
(2), n = 1

Reaction of the hydrobromide of *(1c)*[2,4] with 1,11-dichloro-3,6,9-trioxaundecane afforded a doubly crowned product of the composition *(3)* or *(4)* (m.p. 109—110 °C; sinters at 100 °C) in 20 % yield[3]. From a comparison of the NMR spectra of *(2)* and *(3)* it was assumed that *(3)* was present, yet nanogram thin-layer chromatography of the analytically pure substance (silica gel F_{254}, methanol/water = 1:1) revealed the presence of further components, presumably *(4a)*, *(4b)* or corresponding oligomers.

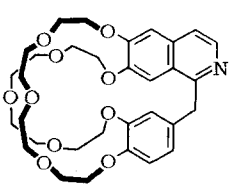
The composition of *(2)* and *(3)* was confirmed by elemental analysis and by high resolution mass spectrometry.



(3), n = m = 1



(4a)



(4b)

The ^{1}H-NMR spectra of *(2)* and *(3)* show besides the characteristic signals for the papaverine moiety[5]—including the benzyl —CH_2— singlet at δ = 4.52 ppm — the characteristic —OCH_2— absorption pattern for the crown ether bridges centered around δ = 3.75 and 3.95 ppm (in $CDCl_3$ and CD_3OD, resp.).

While solid potassium permanganate cannot be dissolved in chloroform with papaverine, this is readily possible with the bridged papaverines *(2)* and *(3)*. As expected the violet color of the solution is much more intense with the doubly crowned ether *(3)* than with *(2)*. *(2)*, of which we obtained gram amounts, reacts with $Ca(SCN)_2 \cdot 4H_2O$ even in the cold in ethyl acetate with formation of mm-long crystalline needles of the 1:1 complex, which contains one molecule of water of crystallization and melts at 173 °C[6]. Its IR spectrum shows a strong and sharp characteristic band at 2055 cm^{-1}, its ^{1}H-NMR spectrum slight shifts of the OCH_2—CH_2O— protons [in $(CD_3)_2SO$].

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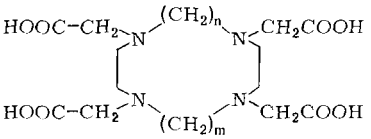
CAS Registry numbers:
(1a), 58-74-2; *(1b)*, 16637-56-2; *(1c)* HBr, 23740-74-1; *(2)*, 60239-23-8; *(3)*, 60239-24-9; *(4a)*, 60239-25-0; *(4b)*, 60239-26-1; 1,11-dichloro-3,6,9-trioxaundecane, 638-56-2

[1] *C. J. Pedersen*, J. Am. Chem. Soc. *89*, 7017 (1967).
[2] *A. Bossi* and *S. Teitel*, J. Org. Chem. *35*, 1684 (1970).
[3] The yields quoted are not optimized.
[4] *J. V. Burba* and *M. F. Murnaghan*, Biochem. Pharmacol. *14*, 823 (1965).
[5] *L. Pohl* and *W. Wiegrebe*, Z. Naturforsch. *20b*, 1032 (1965).
[6] A similar $Ca(SCN)_2$ complex of benzo[15]crown-5 has just recently been reported: *D. G. Parsons* and *J. N. Wingfield*, Inorg. Chim. Acta *18*, 263 (1976).

Complex Formation with Tetraazacycloalkane-*N*,*N*',*N*'',*N*'''-tetraacetic Acids as a Function of Ring Size[**]

By *Hermann Stetter* and *Wolfram Frank*[*]

Reaction of 1,4,7,10-tetraazacyclododecane[1,2], 1,4,7,10-tetraazacyclotridecane[1], and 1,4,8,11-tetraazacyclotetradecane[1] with chloroacetic acid in aqueous alkali medium affords 1,4,7,10-tetraazacyclododecane-*N*,*N*',*N*'',*N*'''-tetraacetic acid *(1)* [m.p. of trishydrochloride 222°C (decomp.)], 1,4,7,10-tetraazacyclotridecane-*N*,*N*',*N*'',*N*'''-tetraacetic acid *(2)* [m.p. of trishydrochloride 185°C (decomp.)], and 1,4,8,11-tetraazacyclotetradecane-*N*,*N*',*N*'',*N*'''-tetraacetic acid *(3)* [m.p. 310°C (decomp.)].



(1), n = m = 2
(2), n = 2, m = 3
(3), n = m = 3

The inorganic salts were separated and purified with the strongly basic ion-exchanger DOWEX 2X8. The capacity of *(1)*, *(2)*, and *(3)* to form complexes was determined by potentiometric titration after a method develop by *G. Schwarzenbach*[3,4]. The results are listed in Table 1. *(1)* is the strongest complexing agent known so far for calcium with a p*K* value of 15.85. In the case of *(2)* stability of the strontium complex (p*K* = 11.70) is outstanding compared with that of the other alkaline earth metal complexes, while *(3)* is characterized by strongly differing complex formation with magnesium and calcium.

Table 1. Basicity and stability constants [H_2O, 20°C, 0.1 N KCl] of some complexes of compounds *(1)* to *(3)*. Values for ethylenediaminetetraacetic acid (EDTA) [4, 5] and 1,2-diaminocyclohexane-*N*,*N*-tetraacetic acid (CyDTA) [6] are given for comparison.

	(1)	*(2)*	*(3)*	EDTA	CyDTA
pK_{Cu}	19.06	17.29	18.60	18.30	21.30
pK_{Ni}	17.25	15.75	15.26	18.40	19.40
pK_{Co}	18.42	14.98	15.00	16.10	18.92
pK_{Zn}	18.90	14.42	15.81	16.10	18.60
pK_{Pb}	19.89	15.63	14.73	18.20	19.68
pK_{Cd}	19.08	16.54	15.53	16.40	19.23
pK_{Mg}	11.03	6.36	*3.02*	9.12	10.32
pK_{Ca}	*15.85*	8.06	*9.48*	11.00	12.50
pK_{Sr}	12.80	*11.70*	6.15	8.80	10.00
pK_{Ba}	—	7.24	4.32	7.78	7.99
$pK^{H}_{H_4Y}$	4.41	3.28	3.46	2.00	2.40
$pK^{H}_{H_3Y}$	4.54	4.59	4.31	2.67	3.50
$pK^{H}_{H_2Y}$	9.73	9.18	9.75	6.13	6.12
pK^{H}_{HY}	11.36	11.22	11.07	10.26	11.70

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CAS Registry numbers:
(1), 60239-18-1; *(1)* 3HCl, 60239-19-2; *(2)*, 60239-20-5; *(2)* 3HCl, 60239-21-6; *(3)*, 60239-22-7; 1,4,7,10-tetraazacyclododecane, 294-90-6; 1,4,7,10-tetraazacyclotridecane, 295-14-7; 1,4,8,11-tetraazacyclotetradecane, 295-37-4; chloroacetic acid, 79-11-8

[1] *H. Stetter* and *K. H. Mayer*, Chem. Ber. *94*, 1410 (1961).
[2] *J. E. Richman* and *Th. J. Atkins*, J. Am. Chem. Soc. *96*, 2268 (1974).
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[4] *S. Chabereck* and *A. E. Martell*, J. Am. Chem. Soc. *74*, 6228 (1952).
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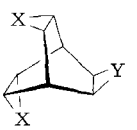
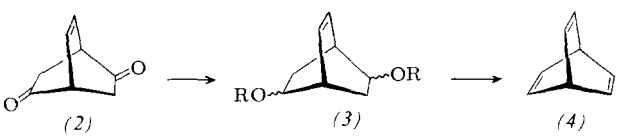
3,7,10-Trioxapentacyclo[3.3.3.$0^{2,4}$.$0^{6,8}$.$0^{9,11}$]-undecane (3,7,10-Trioxatrishomobarrelene)[**]

By *Christian Weitemeyer* and *Armin de Meijere*[*]

Pentacyclo[3.3.3.$0^{2,4}$.$0^{6,8}$.$0^{9,11}$]undecane (trishomobarrelene) *(1)*, X = Y = CH_2[1] is characterized by its extraordinary bridgehead reactivity[2] and its propeller-like molecular shape[3]. For the same reasons heteratrishomobarrelenes, *i.e.* compounds of the type *(1)* with X = CH_2, Y = O, S, NH or Y = CH_2, X = O, S, NH and particularly the C_{3h} symmetrical substances with X = Y = O, S, NH, are also of interest.



(1)



(2) *(3)* *(4)*

(a), R = H
(b), R = C(S)–O–$C_6H_4CH_3$

Preparation of the first representative of this series was accomplished using the barrelene *(4)* as starting material, which according to *Zimmerman et al.*[4] is accessible *via* a nine-step synthesis, but for which we have found a simpler route, namely reduction of the bicyclo[2.2.2]oct-7-ene-2,5-dione *(2)*[5] with $LiAlH_4$ to the bicyclo[2.2.2]oct-7-ene-2,5-diol *(3a)*[6], reaction with 4-methylphenyl chlorothioformate[7] to give the bis(4-methylphenyl)thionocarbonate *(3b)*[6] the thermolysis of which at 170°C affords *(4)* in an overall yield of 20%[8].

In the oxidation of *(4)* with a 50% excess of 3-chloroperoxybenzoic acid in dichloromethane in the presence of potassium hydrogen carbonate, *exo,exo*-3,7-dioxatetracyclo[3.3.2.$0^{2,4}$.$0^{6,8}$]dec-9-ene *(5)* and *endo,exo,syn*-3,7,10-trioxatrishomobarrelene *(6)* were formed. Sublimation of the crude

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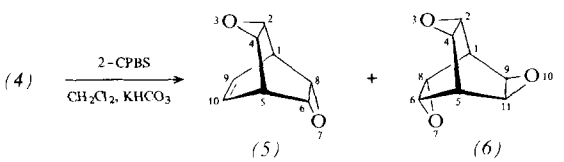
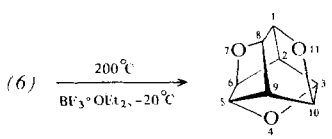
products afforded a mixture of *(5)* and *(6)* in 46% yield [ratio *(5)*:*(6)*=1:1.7]. *(5)* and *(6)* could be obtained in pure form by gas-chromatographic separation, and were then characterized by ^{1}H-NMR spectroscopy[6]. The spectrum (100 MHz, CCl_4) of the dioxatrishomobarrelene *(5)* shows three signals at $\tau = 4.59$ [AA′ part of a AA′XX′ system, 9(10)-H], 6.75 [m, 1(5)-H] and 6.84 [s, 2(4,6,8)-H], that of the trioxide *(6)* (m.p. 202°C, decomp.) only two signals at $\tau = 7.01$ [m, 2(4,6,8,9,11)-H] and 7.14 [m, 1(5)-H].





The thermal rearrangement of *(6)* is interesting: after 3.5 h at 200°C 20% is rearranged to an isomeric compound (m.p. 204°C) the ^{1}H-NMR spectrum of which (100 MHz, $CDCl_3$) shows two signals at $\tau = 5.29$ [AA′ part of a AA′XX′ system, 1(3,5,6,8,10)-H] and 7.60 [m, 2(9)-H], and corroborates the structure of the 4,7,11-trioxapentacyclo[6.3.0.$0^{2,6}$.$0^{3,10}$.$9^{5,9}$]-undecane *(7)*[6]. In the presence of catalytic amounts of boron trifluoride-diethyl ether, rearrangement is already quantitative within 5 min at −20°C. Although *(7)* has a spherical molecular shape very similar to that of *(6)*, its volatility is considerably higher, for the retention time in the gas-chromatogram (SE-30 column) is only about one-half that of *(6)*.

The pentacyclic compound *(7)*, composed exclusively of tetrahydrofuran units, is a 4,7,11-trioxa analog of the well-known (D_3)-trishomocubane[9]. Unlike *(6)*, the hydrocarbon *(1)*, (X=Y=CH_2) does not rearrange into (D_3)-trishomocubane, even in the presence of aluminum bromide[10].

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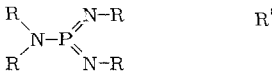
CAS Registry numbers:
(2), 17660-74-1; *(3a)*, 60239-28-3; *(3b)*, 60239-29-4; *(4)*, 500-24-3; *(5)*, 60239-30-7; *(6)*, 60239-31-8; *(7)*, 60239-32-9; 4-methylphenyl chlorothioformate, 937-63-3

[1] *A. de Meijere* and *C. Weitemeyer*, Angew. Chem. *82*, 359 (1970); Angew. Chem. Int. Ed. Engl. *9*, 376 (1970).
[2] *A. de Meijere, O. Schallner*, and *C. Weitemeyer*, Angew. Chem. *84*, 63 (1972); Angew. Chem. Int. Ed. Engl. *11*, 56 (1972).
[3] *W. Spielmann* and *A. de Meijere*, Angew. Chem. *88*, 446 (1976); Angew. Chem. Int. Ed. Engl. *15*, 429 (1976).
[4] *H. E. Zimmerman* and *R. M. Paufler*, J. Am. Chem. Soc. *82*, 1514 (1960); *H. E. Zimmerman, G. L. Grunewald, R. M. Paufler*, and *M. A. Sherwin*, *ibid. 91*, 2330 (1969).
[5] *C. A. Grob* and *A. Weiss*, Helv. Chim. Acta *43*, 1390 (1960). The yield of *(2)* could be increased to 23%.
[6] Elemental analysis, IR, ^{1}H-NMR and mass spectra of all the new compounds are in agreement with the proposed structures.
[7] *H. Gerlach* and *W. Müller*, Helv. Chim. Acta *55*, 2277 (1972).
[8] A two-step synthesis starting from bicyclo[2.2.2]octene [*G. N. Taylor*, J. Org. Chem. *37*, 2904 (1972)] affords *(4)* in only 2% yield. *W. G. Dauben, G. T. Rivers, R. J. Twieg*, and *W. T. Zimmerman*, J. Org. Chem. *41*, 887 (1976), have recently reported a better method of preparation.
[9] *G. R. Underwood* and *Ramamoorthy*, Tetrahedron Lett. *1970*, 4125; *S. A. Godleski, P. von R. Schleyer, E. Osawa*, and *G. J. Kent*, J. C. S. Chem. Commun. *1974*, 976; *P. E. Eaton, R. A. Hudson*, and *C. Giordano*, *ibid. 1974*, 978.
[10] *P. Gölitz* and *A. de Meijere*, unpublished results.

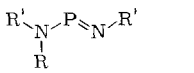
Structure of a Phosphorus-Nitrogen Ylide Having Twofold Coordinated Phosphorus

By *Siegfried Pohl*[*]

While the structure of a phosphorus-nitrogen ylide with pentavalent phosphorus of coordination number three *(1)* has been established by X-ray structure analysis[1], no such study has yet been performed on aminoiminophosphanes[2] of type *(2)* which are liquids under normal conditions.



(1), R = $Si(CH_3)_3$



(2), R = $Si(CH_3)_3$, R′ = $C(CH_3)_3$

The first structure determination on a λ^3-phosphazene was intended primarily to settle any question of an analogy between the bonding of the phosphorus in this compound and that in phosphamethine cyanines and phosphabenzene derivatives and the extent of polarization of the P—N_{imine} bond. The measurements were performed on trimethylsilyl(*tert*-butyl)-amino(*tert*-butyl)iminophosphane *(2)* (m.p. 17 to 19°C)[2] at −10±2°C[3]. The compound forms orthorhombic crystals, Pnma, having $a = 11.228(3)$, $b = 10.063(3)$, $c = 14.282(5)$ Å, $V = 1614$ Å^3, $Z = 4$. The structure was solved with diffractometer data by the direct method of symbolic addition[4].

In the solid the molecule has C_s symmetry. The phosphorus is twofold coordinated to nitrogen atoms; the P—N bond lengths are 1.544(4) and 1.658(4) Å. The P—N_{imine} distance in *(2)* is somewhat greater than in the aminodiiminophosphorane *(1)* (1.503 Å)[1]. Although no comparable data are yet available for phosphorus(III) compounds, the P—N bond lengths reported so far[5] would rule out any significant contribution of a polar resonance structure to *(2)*. Weak d_π-p_π double bond contributions favored by the geometry of the molecule can be assumed for the P—N_{amine} bond. A remarkable feature of *(2)* is the size of the NPN angle (104.9°), due to extensive participation of p orbitals in the phosphorus bonds. Thus the structure determination reveals an extensive analogy with the phosphamethine cyanines and phosphaben-

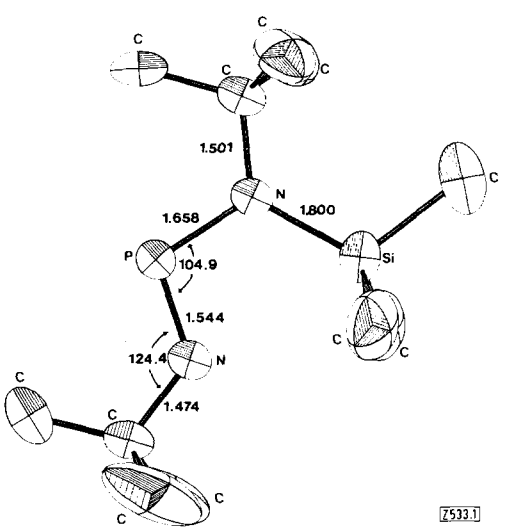


Fig. 1. Molecular structure of trimethylsilyl(*tert*-butyl)amino(*tert*-butyl)iminophosphane in the crystal (vibrational ellipsoids of 50% probability) with bond lengths [Å] and angles [°].

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zene derivatives which also exhibit angles of similar size at the twofold coordinated phosphorus atom[5]. In contrast, the complex $(CO)_5Cr[P(NCR_3)N(SiR_3)_2]$ ($R=CH_3$) which contains an aminoiminophosphane almost identical to *(2)* as ligand is found to have an NPN angle of 119.7° and thus a completely different hybridization at the phosphorus[6].

The other distances and angles in *(2)* correspond to expectation (Fig. 1). The average values of the Si—C and C—C bond lengths are 1.850 and 1.518 Å, respectively. As seen from the size of the vibrational ellipsoids the *tert*-butyl group attached to the imine nitrogen is not completely fixed sterically. Hence localization of the H atoms was feasible only for the other methyl groups.

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CAS Registry number:
(2), 53787-01-2

[1] *S. Pohl, E. Niecke*, and *B. Krebs*, Angew. Chem. 87, 284 (1975); Angew. Chem. Int. Ed. Engl. *14*, 261 (1975).
[2] *O. J. Scherer* and *N. Kuhn*, Angew. Chem. *86*, 899 (1974); Angew. Chem. Int. Ed. Engl. *13*, 811 (1974); J. Organomet. Chem. *82*, C3 (1974); and references cited therein. I am indebted to Prof. Dr. *O. J. Scherer* for supplying the substance.
[3] Transition of the orthorhombic to a monoclinic phase occurs at *ca.* −25°C. No single crystals could be obtained below this temperature.
[4] Syntex P2$_1$ diffractometer, $Mo_{K\alpha}$ radiation; Syntex XTL program system.
[5] *D. E. C. Corbridge:* The Structural Chemistry of Phosphorus. Elsevier, Amsterdam 1974; and references cited therein.
[6] *E. Niecke, G. Ringel*, and *S. Pohl*, to be published.

Differences in the Temperature Dependence of Reaction Parameters in Linear "Free Energy" Relationships[**]

By *Bernd Giese*[*]

The linear free energy relationships (a) have proved their value in the elucidation of reaction mechanisms and in the planning and optimization of synthetic reaction steps[1].

$$\log \frac{k_X}{k_0} = p_r \cdot p_s \qquad \text{(a)}$$

If equation (a) describes the effect of substituents (variation of X) on the rate constant k_X[2] of a series of reactions, then the substituent constants p_s determined in standard reactions and the experimentally determined reactivity differences ($\log k_X - \log k_0$) afford the reaction parameters p_r, which are thus typical selectivity values[3].

It has recently been shown that the selectivities of the radicals R$^\bullet$ in the competition system $BrCCl_3/CCl_4$ depend to such an extent upon the temperature that they coincide in the range 40–80°C and their order is reversed above 80°C[4]. It may therefore be expected that the reaction parameters p_r of various series of reactions become equal at certain temperatures and that the differences in the reaction parameters ($p_{r1} - p_{r2}$) consequently adopt different signs above and below this temperature. This temperature dependence of the reaction parameters can also be demonstrated with the aid of the radical halogen abstractions in the competition system $BrCCl_3/CCl_4$.

$$RCl \xleftarrow[k_{Cl}]{CCl_4} R^\bullet \xrightarrow[k_{Br}]{BrCCl_3} RBr$$

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The Taft-Hancock equation (b) has here proved its value as a linear free energy relationship[5]:

$$\log \frac{k_R}{k_{CH_3}} = \delta_X \cdot E_s^c \qquad \text{(b)}$$

where δ_X (X = Br, Cl) are the reaction parameters and E_s^c the ateric substituent constants for the different radicals R$^\bullet$[6].

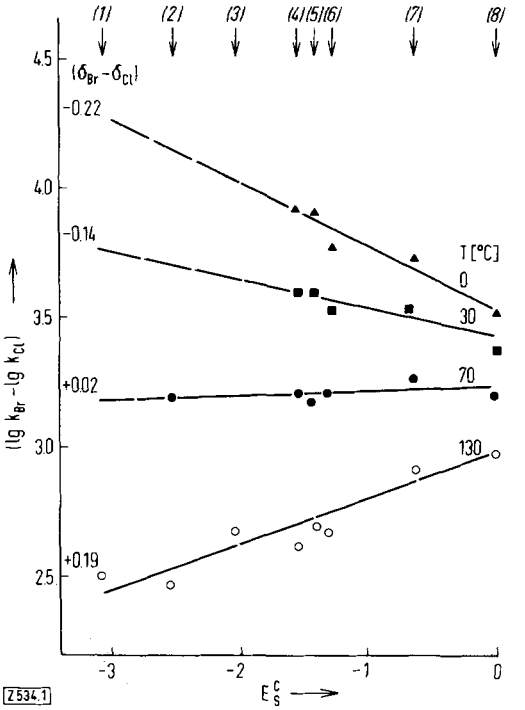

Fig. 1. Dependence of the differences in reactivity ($\log k_{Br} - \log k_{Cl}$) for the alkyl radicals *(1)*–*(8)* on the steric E_s^c constants between 0 and 130°C. *(1)*, $CH_3\dot{C}(C_2H_5)_2$; *(2)*, $C_8H_{17}\dot{C}(CH_3)_2$; *(3)*, $C_4H_9C(CH_3)_2\dot{C}H_2$; *(4)*, c-$\dot{C}_7H_{13}$; *(5)*, c-$\dot{C}_6H_{11}$; *(6)*, 2-$\dot{C}_8H_{17}$; *(7)*, 1-$\dot{C}_7H_{15}$; *(8)*, $\dot{C}H_3$.

The straight lines in Figure 1 show that in the temperature range of 0 to 130°C the radical selectivities ($\log k_{Br} - \log k_{Cl}$) depend upon the group size of the radicals *(1)* to *(8)* in a manner described by the Taft-Hancock relationship (b). Polar effects do not play any role, although the electrophilic CCl_3 radical[8] is displaced by alkyl radicals of various nucleophilicities[9] in these radical substitution reactions[7]. Release of the same CCl_3 radical on abstraction of bromine and chlorine in the competition system $BrCCl_3/CCl_4$ leads to extensive compensation of the polar effects in the transition states *(9)* and *(10)*[10] so that essentially only the differing steric interactions of bromine and chlorine transfer onto the radicals *(1)* to *(8)* become effective.

$$[\overset{\delta+}{R}\cdots\cdots Br\cdots\overset{\delta-}{C}Cl_3]^\bullet \qquad [\overset{\delta+}{R}\cdots Cl\cdots\overset{\delta-}{C}Cl_3]^\bullet$$

(9) *(10)*

The slopes of the straight lines in Figure 1 indicate the differences in the reaction parameters ($\delta_{Br} - \delta_{Cl}$). Their opposing signs at 0°C [$(\delta_{Br} - \delta_{Cl}) = -0.22$] and 130°C [$(\delta_{Br} - \delta_{Cl}) = +0.19$] show that the reaction parameters δ_{Br} and δ_{Cl} vary differently with temperature and are equal at about 60°C. This accords with the experimentally determined isoselective temperature (T_{is}) at which the radical selectivities coincide in the $BrCCl_3/CCl_4$ system[11]. As for the selectivities[4] a comparison of the reaction parameters leads to false conclusions if the isoselective temperature of the competing series of reactions lies below the temperature of measurement. The interpretation of reaction parameters therefore requires at

least a qualitative knowledge of their variation with temperature.

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(1), 19067-45-9; (2), 58281-61-1; (3), 22904-47-8; (4), 4566-80-7; (5), 3170-58-9; (6), 3268-43-7; (7), 3356-67-0; (8), 2229-07-4

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[4] B. Giese, Angew. Chem. 88, 159 (1976); Angew. Chem. Int. Ed. Engl. 15, 173 (1976).
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Chemical Waves in the 2,4-Pentanedione/Potassium Bromate System

By *Wolfgang Jessen*, *Heinrich G. Busse*, and *Bent Havsteen*[*]

A homogeneous solution in which a chemical reaction is taking place usually remains monodisperse. We now report an exception[1].

Into the lid of a Petri dish (90 mm diameter) at 10 °C were successively introduced: 2.0 M H_2SO_4 (7.5 ml), 0.3 M $KBrO_3$ (3.75 ml), H_2O (3.75 ml), and tris(2,4-pentanedionato)manganese(III) (81.4 mg). After mixing, the bottom of the Petri dish is placed in the solution. Glass spacers ensure that there is a 2 mm-thick liquid layer between the two glass surfaces.

After about 10 min, a small yellow spot (pacemaker) suddenly appears in the initially homogeneous solution which is kept at room temperature. The spot steadily expands while the remaining solution stays colorless. Once it has reached a diameter of about 10 mm, the solution decolorizes starting from the center of the circle, while the periphery continues to grow. After a brief pause a yellow spot is reformed in the center of the ring, and a second ring migrates through the solution. Instead of a system of concentric rings, spirals may appear or ring formation may simultaneously occur at several places in the solution to give a pattern of the kind shown in Figure 1. This Figure shows the state of a solution 20 min after the admixture of 2,4-pentanedione (as its Mn^{III} complex). About 40 min later, the pattern had disappeared and the solution was again monodisperse. The solution remained clear all the time; toward the end of the reaction only a slight cloudiness appeared but no precipitate was formed.

Compared with other known systems[1], the one described here has the advantage that it neither forms a precipitate nor liberates a gas. Consequently, it can also be contained in a sealed vessel. We believe it to be a suitable model for the experimental and theoretical study of chemical oscillations in time and space. At present, however, too little is known about the reaction course to explain the observed phenomena.

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Fig. 1. Instantaneous photograph of an oscillating chemical system which forms a pattern varying in space and time. The solution (see text for details) is located in a Petri dish standing on light-sensitive paper (Agfa Brovira BH 111). To increase the contrast a cobalt glass was placed between the light source (normal 100 W light bulb) and the Petri dish.

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$KBrO_3$, 7758-01-2; tris(2,4-pentanedionato)manganese(III), 14284-89-0

[1] Cf. A. T. Winfree, Sci. Am., June 1974, p. 82.

C-Substitution of Nucleosides with the Aid of the Eschenmoser Sulfide Contraction[1]

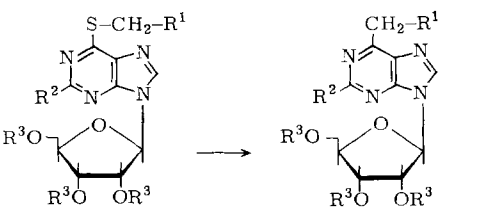
By *Helmut Vorbrüggen* and *Konrad Krolikiewicz*[*]

Among the numerous chemical modifications of nucleosides and nucleotides suitable for preparing analogs of biological interest, very little attention has so far been paid to C-substitution in the α- or γ-position to the heterocyclic nitrogen atoms[2].

We have therefore applied the Eschenmoser sulfide contraction[3] to the readily accessible *S*-alkyl derivatives[4] of 6-thiopurine and of 2- or 4-thiopyrimidine nucleosides.

The *S*-alkyl derivatives *(1)* of 6-thiopurine nucleosides reacted with strong bases and triphenylphosphane to give the *C*-alkylated nucleosides *(2)*, generally in good yield. The products were hydrolyzed to give the free crystalline compounds *(3)*[5] (see Table 1 for details).

The 6-phenacylthiopurine afforded, analogously to *(1a)*, 6-phenacylpurine (m.p. 248 °C) in 88 % yield.



(1) → *(2)*, R^3 = Ac, $Si(CH_3)_3$; *(3)*, R^3 = H

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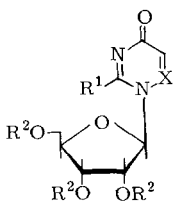
Table 1. 6-C-substituted purine nucleosides.

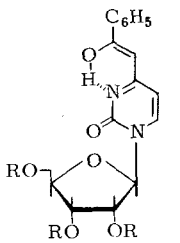
	(1)		Reaction conditions		(3)		
R^1	R^2	R^3	(1)→(2)	(2)→(3)	R^2	Yield [%]	M.p. [°C]
(a) COC_6H_5	H	Ac	72 h [a]	[c]	H	77	218—220
(b) $COOC(CH_3)_3$	H	Ac	[b]	[c]	H	80	—
(c) C_6H_4—NO_2-(1,4)	H	Ac	[b]	[c]	H	78	192—194
(d) COC_6H_5	$NHSi(CH_3)_3$	$Si(CH_3)_3$	16 h [a]	CH_3OH/Δ	NH_2	72	147—150

[a] 0.1 equiv. $(CH_3)_3COK$/4 equiv. $P(C_6H_5)_3$/xylene/Δ.
[b] 2 equiv. $LiN[CH(CH_3)_2]_2$/2 equiv. $P(C_6H_5)_3$/1 equiv. HMPT/THF/−70°C → +24°C.
[c] CH_3OH/NH_3/18 h/24°C.

On refluxing for 2 h in DMF the *S*-phenacyl derivatives of 2-thio- and 2-thio-6-azauridine 2',3',5'-tri-*O*-benzoate[6] furnished the crystalline benzoylated 2-phenacyl derivatives *(4a)* [m.p. 120 to 122°C, 76% yield] and *(4b)* [m.p. 170 to 173°C, 83% yield]. On hydrolysis with CH_3OH/NH_3/18 h/24°C *(4a)* is transformed in 90% yield into the free phenacyl derivative *(5a)*, m.p. 204 to 208°C, whereas *(4b)* undergoes a retroaldol cleavage to afford the free 2-methyl derivative *(5b)*, m.p. 183 to 185°C, in 90% yield.



(4a), $R^2 = COC_6H_5$, $R^1 = CH_2COC_6H_5$, X = CH
(4b), $R^2 = COC_6H_5$, $R^1 = CH_2COC_6H_5$, X = N
(5a), $R^2 = H$, $R^1 = CH_2COC_6H_5$, X = CH
(5b), $R^2 = H$, $R^1 = CH_3$, X = N



(6a), R = COC_6H_5
(6b), R = H

In analogous manner, 2 hours' refluxing of the *S*-phenacyl derivative of 4-thiouridine 2',3',5'-tri-*O*-benzoate[7] in DMF gave the benzoylated 4-phenacyl derivative *(6a)* [m.p. 213 to 215°C][5] in 66% yield, but 6 hours' refluxing in xylene with 0.1 equiv. $(CH_3)_3COK$/4 equiv. triphenylphosphane afforded the same product in 90% yield. Saponification with CH_3OH/NH_3 gave the free phenacyl derivative *(6b)*, m.p. 182 to 184°C, in 90% yield.

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(1a), 60363-84-0; *(1b)*, 60363-85-1; *(1c)*, 60363-86-2; *(1d)*, 60363-87-3; *(3a)*, 60363-88-4; *(3b)*, 60363-89-5; *(3c)*, 60363-90-8; *(3d)*, 56987-12-2; *(4a)*, 60363-91-9; *(4b)*, 60363-92-0; *(5a)*, 60363-93-1; *(6a)*, 60363-95-3; *(6b)*, 60363-96-4; 2-thiouridine 2',3',5'-tri-*O*-benzoate *S*-phenacyl derivate, 60363-97-5; 2-thio-6-azauridine 2',3',5'-tri-*O*-benzoate S-phenacyl derivative, 60363-98-6; 4-thiouridine 2',3',5'-tri-*O*-benzoate *S*-phenacyl derivative, 60363-99-7

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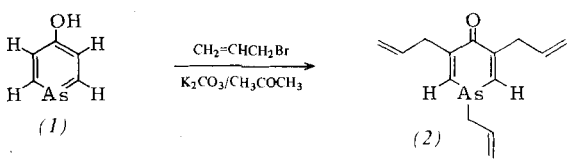
Allylation of 4-Hydroxyarsenin—Arsenic-Carbon Hetero-Cope Rearrangement

By *Gottfried Märkl* and *Jang B. Rampal*[*]

Dedicated to Professor Leopold Horner on the occasion of his 65th birthday

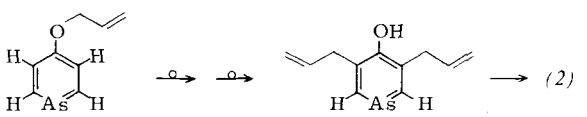
We recently reported 4-hydroxyarsenin *(1)* (arsaphenol)[1], the first simple heterocyclic phenol, which exists only in the hydroxy form. On reaction with allyl bromide in boiling acetone (12 h in the presence of K_2CO_3) according to the general synthesis of allyl phenyl ethers[2], *(1)* gives 1,3,5-triallyl-1-arsacyclohexa-2,5-dien-4-one *(2)* as the sole product.



(1) *(2)*

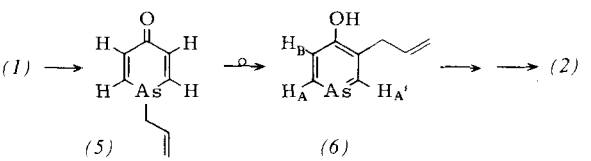
There are three possible pathways for the formation of *(2)*:

a) Formation of the allyl ether *(3)*, subsequent Claisen *ortho*-allyl ether rearrangement, and repetition of this reaction sequence leads to 3,5-diallyl-4-hydroxyarsenin *(4)*. Renewed allyl ether formation followed by *para*-Claisen rearrangement or direct allylation at the arsenic can give *(2)*.



(3) *(4)*

(b) Direct *C*-allylation in the 2,5-position and subsequent allylation at the arsenic.



(5) *(6)*

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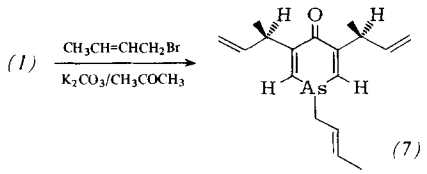
(c) Allylation at the arsenic to form *(5)*, [3s,3s]-sigmatropic shift of the allyl group into the 3- or 5-position as a hetero-Cope rearrangement to give *(6)*, and repetition of this reaction sequence.

Pathway (b) can be ruled out: crotyl bromide reacts with *(1)* to give *(7)* in which the crotyl moieties in positions



3 and 5 have undergone inversion. This inversion is possible only by way of *ortho*-Claisen rearrangement corresponding to *(3)* → *(4)* or by hetero-Cope rearrangement corresponding to *(5)* → *(6)*. Pathway (a) is rather unlikely since non-catalytic allyl ether rearrangement of the phenols[3] and the 2- or 4-hydroxypyridines[4] by a Claisen type mechanism requires more drastic conditions (150 to 250°C) than formation of *(2)* and *(4)*.

Reaction of *(1)* with allyl bromide in acetone at 25°C (24 h in the presence of K_2CO_3) also gives only compound *(2)*. Formation of *(3)* is not observed. Changing the solvent (from protic to dipolar/aprotic), the allyl halide, or the base had no effect.

After 4 hours' reaction at 25°C the product is a mixture of *(2)*, *(5)*, and 1,3-diallyl-1-arsacyclohexa-2,5-dien-4-one *(8)*, which was analyzed by ^{1}H-NMR and mass spectrometry (*m/e* = 196; 236; 276).

After 1 hour's reaction at 25°C the major product is *(5)*. It could not be prepared pure, since it rearranges quantitatively to *(6)* within a few hours at as low a temperature as 0 to 5°C.

Since *(5)*, *(6)*, and *(8)* can be converted into *(2)* under the same conditions as *(1)*, these compounds are intermediates of the reaction *(1)* → *(2)*. The formation of *(2)* is thus the result of two exceptionally easy hetero-Cope rearrangements, *i.e.* of [3s,3s]-shifts of the allyl moieties from the arsenic to C-3 and C-5 in compounds *(5)* and *(8)* followed by *As*-allylation of *(4)*. The driving force of these rearrangements is probably the aromatization of the arsacyclohexadienone intermediates. The rearrangement products are then again susceptible to *As*-allylation.

Table 1. Properties of the compounds *(2)*, *(5)*, *(6)*, and *(7)*.

(2): Yield 30%, pale yellow oil after chromatography on SiO_2/benzene b.p. 115°C/0.01 torr.—^{1}H-NMR ($CDCl_3$): ring-H: δ = 7.35 ppm (s); As—CH_2: 2.66 ppm, 2H (d); =C—CH_2: 3.33 ppm, 4H (d); vinyl-H: 4.70—6.25 ppm, 9H (m).—IR (film): $\nu_{C=O}$ = 1615 cm^{-1}.—UV (ethanol): λ_{max} = 316 nm (ε = 6000); 234 nm, shoulder (ε = 7200).—MS (CH5, 70 eV): M^+ [$C_{14}H_{17}AsO_2$], *m/e* = 276 (rel. int. 27%); [M − C_3H_5]$^+$ 235 (74%); [235 − C_3H_6]$^+$ 193 (100%).

(5): ^{1}H-NMR ($CDCl_3$): ring-H: AB spectrum, J_{AB} = 12 Hz; H_A = 7.66 ppm; H_B = 6.86 ppm; As—CH_2: 2.66 ppm, $J_{H/H}$ = 7 Hz; vinyl-H: 4.70—6.10 ppm, 3H (m).

(6): colorless oil, b.p. 85°C/0.01 torr.—^{1}H-NMR ($CDCl_3$): H_A: δ = 9.60 ppm (s); H_A/H_B: AB-spectrum, $J_{H/H}$ = 11 Hz; H_A: 9.36 ppm; H_B: 7.53 ppm; vinyl-H: 4.90—6.20 ppm; As—CH_2: 3.66 ppm (d), $J_{H/H}$ = 6 Hz.—MS: M^+ [C_8H_9AsO], *m/e* = 196 (57%); [196 − C_3H_4]$^+$ 156 (100%); [156 − CO]$^+$ 128 (26%).

(7): Yield 27%; pale yellow oil after chromatography on SiO_2/benzene; b.p. 120°C/0.01 torr.—^{1}H-NMR ($CDCl_3$): ring-H: δ = 7.16 ppm (s); >CH—CH_3: 2 doublets at 1.03 and 1.10 ppm, 6H; $J_{H/H}$ = 7 Hz; ≥C—H: 2 quartets at 3.80, 3.90 ppm, 2H; $J_{H/H}$ = 7 Hz; =CH—CH_3: 1.53 ppm, 3H; $J_{H/H}$ = 4 Hz; As—CH_2: 2.43 ppm, 2H; $J_{H/H}$ = 6 Hz; vinyl-H: 4.70—6.20 ppm, 8H (m).—IR (film): $\nu_{C=O}$ = 1620 cm^{-1}.—UV (ethanol): λ_{max} = 326 nm (ε = 4500); 232 nm, shoulder (ε = 6700).—MS: M^+ [$C_{17}H_{23}AsO$] *m/e* = 318 (21%); [M − C_4H_6]$^+$ 264 (99%); [M − C_4H_7]$^+$ 263 (100%); [263 − C_4H_6]$^+$ 209 (26%); [263 − C_4H_8]$^+$ 207 (39%).

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(1), 56598-57-3; *(2)*, 60479-91-6; *(3)*, 60479-92-7; *(4)*, 60479-93-8; *(5)*, 60479-94-9; *(6)*, 60479-95-0; *(7)*, 60479-96-1; CH_2=$CHCH_2Br$, 106-95-6; CH_3CH=$CHCH_2Br$, 4784-77-4

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The Thionitrosyl Cation NS^+ as a Synthetic Reagent[**]

By *Rüdiger Mews*[*]

Dedicated to Professor Oskar Glemser on the occasion of his 65th birthday

The thionitrosyl compounds ("thiazyl salts") $NS^+MF_6^-$ *(1)* were obtained by *Glemser* and *Koch*[1] on reaction of thiazyl fluoride NSF with the Lewis acids MF_5 (M = As, Sb). For preparative purposes these salts are best synthesized in liquid sulfur dioxide; purification of *(1a)* can be accomplished by sublimation at oil-pump vacuum (40°C), and that of *(1b)* by heating to 100°C and recrystallization of the residue from SO_2/SO_2ClF[2].

$$NSF + MF_5 \xrightarrow{SO_2\ liq.} NS^+MF_6^-$$

(1a), M = As; *(1b)*, M = Sb

The cation of *(1)* is readily attacked by anions or nucleophiles. In the absence of other reactants the salts *(1)* can be stored indefinitely in dry glass containers.

We have hitherto examined three possible modes of reaction:

1) Reaction of the thionitrosyl cation with anions:

$$\underset{(2)}{(1a) + NO^+CF_3SO_3^-} \xrightarrow[-NO^+AsF_6^-]{SO_2\ liq.} \underset{(3)}{NS^+CF_3SO_3^-}$$

The colorless product *(3)*, m.p. 120°C, is extremely sensitive to hydrolysis. Comparison of the Raman spectra of *(2)* and *(3)* indicates the solid to have an ionic structure (νSN 1443 cm^{-1}). Its ease of sublimation shows the compound to exist as the monomer, at least in the gas phase.

2) Reaction of the thionitrosyl cation with nucleophiles[3]:

$$(1) + S_4N_4 \xrightarrow{SOCl_2} \underset{(4)}{\{S_4N_4 \cdot (NS^+MF_6^-)\}} \longrightarrow S_5N_5^+MF_6^-$$

(5a), M = As; *(5b)*, M = Sb

Insertion of a SN unit into S_4N_4 affords the yellow pentathiazyl salts *(5a)* and *(5b)*, m.p. 267 and 175°C, respectively, in

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yields of 80%. Nothing can be said about the nature of the primary product *(4)*; both a simple addition of the nucleophile to the sulfur of *(1)* and a cycloaddition are conceivable.

When carried out in liquid SO_2 the reaction affords a black solid *(6)*, dec. 110°C, together with other unidentified substances.

$$(1a) + S_4N_4 \xrightarrow{SO_2\ liq.} (S_5N_5^+AsF_6^-)_x$$
(6)

Elemental analysis indicates the composition $S_5N_5^+AsF_6^-$; the IR spectrum contains strong bands at 700 ($\nu_3AsF_6^-$) and 850 cm^{-1} (br). The latter finding suggests that *(6)* is polymeric. The ratio (NS): AsF_6 in *(6)* can be varied by changing the stoichiometry; a drop in this ratio (increase in charge on the polymer) is associated with a shift of νNS to higher wave numbers.

3) Reaction of the thionitrosyl cation with polar bonds:

$$(1) + \overset{\delta+}{Cl}S-\overset{\delta-}{Cl} \xrightarrow{SO_2\ liq.} N(SCl)_2^+MF_6^-$$
(7a), M = As; *(7b)*, M = Sb

The first synthesis of the cation in *(7)* was accomplished starting from NSF_3 and BCl_3[4], and it is also obtainable from SCl_2, $(NSCl)_3$, and MCl_3[5]. According to the formulation adopted here, the compounds *(7)* can be regarded as derivatives of $ClSN{=}SCl_2$ or $ClSN{=}SClF$; however, reactions between *(7)* and NOCl only lead to decomposition products. The reaction of *(1)* with SCl_2 can be generalized for sulfenyl chlorides: the salts $[CF_3SNSCl]^+MF_6^-$ and $[(CF_3)_2C{=}N{-}SNSCl]^+MF_6^-$ could be prepared from CF_3SCl and $(CF_3)_2C{=}N{-}SCl$, respectively, and *(1)*[6].

Experimental

For the preparation of thionitrosyl trifluoromethanesulfonate *(3)*, compound *(1a)* is stirred with a slight excess of *(2)* for 24 h at room temperature in liquid SO_2. After removal of the SO_2, compound *(3)* can be isolated from the residue by sublimation.

For the preparation of the pentathiazyl salts *(5)*, compound *(1)* and S_4N_4 (molar ratio 1:1) are stirred in $SOCl_2$ at room temperature until the initially dark solution over the precipitated salt turns yellow. *(5)* is separated by filtration and washed with $SOCl_2$.—The analogous reaction performed in SO_2 affords, in the course of several days, compound *(6)* which is insoluble in SO_2; it is freed from side-products by washing with that solvent (yield *ca.* 60%).

Compounds *(7)* are formed in liquid SO_2 at room temperature (reaction time *ca.* 10 h). The solvent and a slight excess of sulfenyl chloride are removed *in vacuo*. The salts are left behind in analytically pure form (quantitative yield).

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CAS Registry numbers:
(1a), 31967-65-4; *(1b)*, 34770-46-2; *(2)*, 51637-52-6; *(3)*, 60525-76-0; *(5a)*, 60537-78-2; *(5b)*, 60537-79-3; *(6)*, 60537-77-1; *(7a)*, 60563-08-8; *(7b)*, 60563-09-9; S_4N_4, 28950-34-7; ClSCl, 10545-99-0

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[2] Raman spectrum of $NS^+SbF_6^-$: 1448 (νSN), 657 (ν_1SbF_6), 563 (ν_2SbF_6), 284 cm^{-1} (ν_5SbF_6).
[3] The NS^+ ion was postulated as an intermediate in the preparation of the pentathiazyl salts *(5)* from S_4N_4, $(NSCl)_3$, and MCl_3 or MCl_5 in $SOCl_2$ [*A. J. Banister* and *H. G. Clarke*, J. Chem. Soc. Dalton *1972*, 2661]; however, it cannot be isolated in this way.
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[5] *O. Glemser* and *J. Wegener*, Inorg. Nucl. Chem. Lett. *7*, 623 (1971).
[6] *R. Mews, H. Steinbeisser*, and *J. Varwig*, to be published.

1,3,2λ²,4-Diazaphosphoniaaluminatacyclobutane: A Cyclic Zwitterion Having Twofold Coordinated Phosphorus[1]

By *Edgar Niecke* and *Rainer Kröher*[*]

Dedicated to Professor Oskar Glemser on the occasion of his 65th birthday

Phosphorus-nitrogen compounds having twofold coordinated phosphorus are known in the form of aminophosphanylium salts *(1)* and iminophosphanes *(2)*.

$$[-\overset{\oplus}{P}-N<]\ X^{\ominus} \qquad -P{=}N-$$
(1) *(2)*

We have now succeeded in synthesizing the zwitterionic compounds *(4)* and *(5)* by reaction of bis(trimethylsilyl)-amino(trimethylsilylimino)phosphane *(3)* with aluminum trichloride.

$$2\ R_2N{-}P{=}NR + Al_2Cl_6 \longrightarrow 2\ R_2N{-}\overset{\oplus}{P}{-}N(R)(\overset{\ominus}{Al}Cl_3) \longrightarrow$$
(3) *(4)*

$$2\ R{-}N\langle P\rangle N{-}R + 2\ RCl$$
$$Al^{\ominus}(Cl)(Cl)$$
(5)

R = $Si(CH_3)_3$

(4) and *(5)* are colorless solids which are extremely sensitive to hydrolysis. Above 40°C *(4)* undergoes significant transformation into *(5)*, which itself is remarkably thermostable (m.p. 103°C). Four-membered phosphorus heterocycles having zwitterionic structure were formerly only known with fourfold and sixfold coordinated phosphorus[2].

The zwitterionic structure of the compounds is evidenced by the downfield shift of the ^{31}P-NMR resonance signal on going from *(3)* [$\delta = -325.5$ ppm[3]] to *(4)* [$\delta = -450.4$ ppm] and on comparison of *(5)* [$\delta = -379.3$ ppm] with the isoelectronic 1,3,2,4-diazaphosphasilacyclobutan-2-ylium cation *(7)* [$\delta = -343.1$ ppm], a representative of the class of compounds *(1)*. Compound *(7)* could be prepared from the chlorophosphane *(6)*[4] by reaction with aluminum trichloride.

$$2\ R{-}N\langle P(Cl)\rangle N{-}R + Al_2Cl_6 \longrightarrow 2\ R{-}N\langle \overset{\oplus}{P}\rangle N{-}R\ [AlCl_4]^{\ominus}$$
$$Si(Cl)(Cl)$$
(6) *(7)*

Compound *(5)* reacts with *tert*-butyl azide to give the spiroheterocycle *(9)*, which is to be regarded as the P—N cycloaddition product of the iminophosphorane *(8)* and *tert*-

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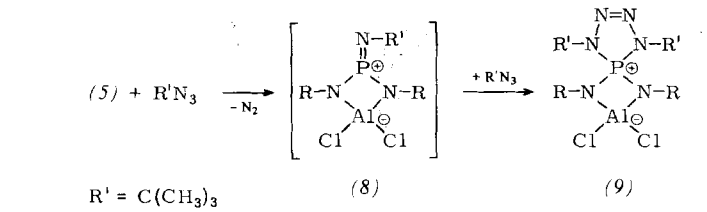
butyl azide. Attempts to liberate the threefold coordinated phosphorus compound *(8)* by heating the adduct *(9)* were unsuccessful.



(5) + $R'N_3$ $\xrightarrow{-N_2}$ *(8)* $\xrightarrow{+R'N_3}$ *(9)*

$R' = C(CH_3)_3$

[1] Investigations on Phosphazenes with Coordination Numbers 2 and 3, Part 10. This work was supported by the Deutsche Forschungsgemeinschaft.—Part 9: *E. Niecke, W. Flick,* and *S. Pohl,* Angew. Chem. *88,* 305 (1976); Angew. Chem. Int. Ed. Engl. *15,* 309 (1976).

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[4] *E. Niecke* and *W. Bitter,* Chem. Ber. *109,* 415 (1976).

[5] Mass spectrum (70 eV) *m/e: (5)* M 302 (8%), M−CH_3 287 (100%); *(9)* M 472 (47%), M−(CH_3, C_4H_8) 401 (100%); *(4)* shows essentially the same fragmentation pattern as *(5)*, and *(7)* that of *(6)*.

Table 1. NMR data [a] and characteristic IR absorptions [b] of the compounds *(4)*, *(5)*, *(7)*, and *(9)*.

	$\delta^{31}P$ [ppm] [c]	$\delta^{1}H$ [ppm] [c]		$^4J_{HP}$ [Hz]		IR [cm^{-1}]
		$SiCH_3$	CCH_3	PNSiCH	PNCCH	
(4)	−450.4	−0.29 (d) [d]	—	1.75	—	ν_{as}(PNSi), ν_{as}(SiNSi): 1035, 995
		−0.50 (d)	—	1.20	—	
(5)	−379.3	−0.29 (d)	—	0.68	—	ν_{as}(PN-Ring): 1074,
(7)	−343.1	−0.51 (d)	—	0.65	—	ν_{as}(PN-Ring): 1005, $\nu_3(AlCl_4)^-$: 490
(9)	− 3.8	−0.17 (d)	−1.62	0.57	<0.1	ν_{as}(PN-Ring): 1076, ν(N=N): 1455 [e]

[a] 30% solution in $C_6H_5CH_3$ for *(4)*, in CH_2Cl_2 for *(5)*, *(7)*, and *(9)*. [b] Nujol mull. [c] $\delta(^{31}P, {}^{1}H) < 0$ signifies lower field than the standard (H_3PO_4 external or TMS international). [d] $[(CH_3)_3Si]_2N$. [e] Raman.

The structure of *(9)* is supported by the appearance of a strong Raman line at 1445 cm^{-1} [ν(N=N)] and the equivalence of the signals of the *tert*-butyl protons in the ^{1}H-NMR spectrum (cf. Table 1). The compositions of all the compounds are confirmed by the results of elemental analysis and, in the case of *(5)* and *(9)*, by the appearance of the molecular ion as the highest peak in the mass spectrum[5].

Procedures:

(4) and *(5)*: A solution of *(3)* (28 g, 0.1 mol) in toluene (30 ml) is added dropwise to a stirred and cooled (0 °C) suspension of $AlCl_3$ (13.5 g, 0.1 mol) in toluene (30 ml) with rigorous exclusion of moisture. The solution is stirred for 3—4 h at room temperature and then briefly heated to 40 °C. The solvent and the trimethylsilyl chloride are drawn off *in vacuo*. The residue is taken up in toluene (50 ml), crystallized at −20 °C, and purified by a single recrystallization. Yield 31 g (75%) of *(4)*.

On thermolysis at 70 °C/0.1 torr in a sublimation apparatus, compound *(4)* (20.5 g, 0.05 mol) furnishes *(5)* (13 g), which is purified by another sublimation step at 60 °C/0.1 torr. Yield 11.5 g (78%) of *(5)*, m.p. 103 to 104 °C.

(7): Compound *(6)* (6.8 g, 0.02 mol) is added dropwise to a stirred and cooled (0 °C) suspension of $AlCl_3$ (2.5 g, 0.02 mol) in toluene (10 ml). Compound *(7)* precipitates as a white solid. The solution is stirred until it is colorless. The solid is filtered off on a frit, washed several times with toluene, recrystallized from dichloromethane at −20 °C, and vacuum dried. Yield 7.4 g (78%) of *(7)*, dec. p. 70 °C.

(9): *tert*-Butyl azide (5 g, 0.05 mol) is added to a stirred solution of *(5)* (6.1 g, 0.02 mol) in toluene (30 ml) at room temperature; slight warming occurs and N_2 is liberated. When evolution of N_2 has ceased the solvent and unreacted azide are removed *in vacuo*. The residue is recrystallized from toluene at −70 °C and vacuum dried. Yield 7.9 g (84%) of *(9)*, m.p. 95 °C (dec.).

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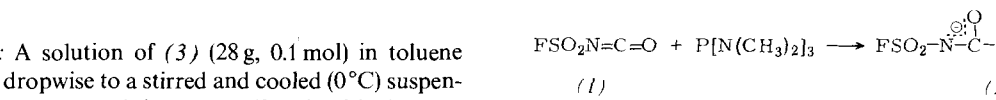
(3), 50732-21-3; *(4)*, 60746-40-9; *(5)*, 60746-41-0; *(6)*, 58971-97-4; *(7)*, 60746-43-2; *(9)*, 60746-44-3; Al_2Cl_6, 13845-12-0; $C(CH_3)_3N_3$, 13686-33-4; ^{31}P, 7723-14-0

Phosphorus Betaines[**]

By *Herbert W. Roesky* and *Georg Sidiropoulos*[*]

Dedicated to Professor Oskar Glemser on the occasion of his 65th birthday

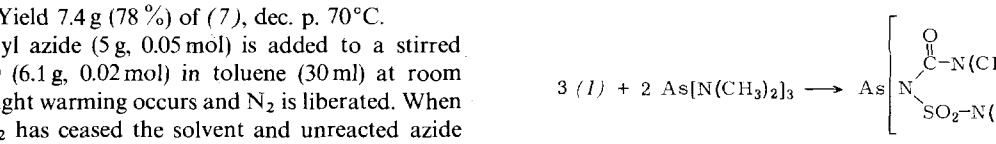
Surprisingly, very stable zwitterions *(2)* can be obtained from tertiary phosphanes and fluorosulfonyl isocyanate *(1)*.



$FSO_2N{=}C{=}O + P[N(CH_3)_2]_3 \longrightarrow FSO_2{-}\overset{\ominus}{N}{-}\overset{O}{\overset{\|}{C}}{-}\overset{\oplus}{P}[N(CH_3)_2]_3$

(1) *(2)*

While *(1)* and water react with explosive violence and its adduct with a tertiary amine proves to be unstable[1], compound *(2)* can be recrystallized from water without decomposition. Strong evidence supporting the betaine structure was obtained from IR and NMR studies[2]: in the IR spectrum the C=O stretching frequency is observed at 1620 wave numbers. The ^{19}F-NMR spectrum contains a doublet due to coupling with the phosphorus atom ($\delta_F = -50.52$ ppm, $CFCl_3$ as external standard, $J_{F-P} = 22$ Hz). Owing to coupling between the fluorine atom and the protons the ^{31}P-NMR spectrum displays a multiplet ($\delta_P = -34.2$ ppm in CH_3CN, 85% H_3PO_4 as external standard). The chemical shift lies in the range expected for tetracoordinated phosphorus. The ^{1}H- and ^{13}C-NMR data confirm the structure *(2)*, and elemental analysis indicates the empirical formula $C_4H_{18}FN_4O_3$.



3 *(1)* + 2 $As[N(CH_3)_2]_3 \longrightarrow As\left[N(SO_2{-}N(CH_3)_2)(C(=O){-}N(CH_3)_2)\right]_3 + AsF_3$

(3)

A corresponding betaine can be prepared with $(C_6H_5)_3P$. Tertiary arsanes behave completely differently: Reaction of

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[**] This work was supported by gifts of chemicals from Hoechst AG.

(1) and $As[N(CH_3)_2]_3$ proceeds *via* rearrangement to give *(3)* and AsF_3.

Procedure:

Synthesis of *(2)*: Compound *(1)* (0.1 mol, 12.5 g) dissolved in CH_2Cl_2 (50 ml) and $P[N(CH_3)_2]_3$ in CH_2Cl_2 (50 ml) are added from two dropping funnels to vigorously stirred CH_2Cl_2 (150 ml) at −30 °C in a 500-ml three-necked flask. When addition is complete, the mixture is warmed to room temperature and the solvent removed under vacuum. The residue is a light brown solid which is recrystallized from CH_3CN or H_2O. M.p. 140 to 142 °C.

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CAS Registry numbers:
(1), 1495-51-8; *(2)*, 21904-69-8; *(3)*, 60734-50-1; $P[N(CH_3)_2]_3$, 1608-26-0; $As[N(CH_3)_2]_3$, 6596-96-9; ^{31}P, 7723-14-0

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[2] We are grateful to Dr. *E. Niecke*, Göttingen, for NMR measurements.

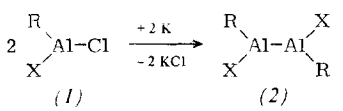
The Al—Al Bond as a Readily Accessible Structural Unit in Organometallic Compounds

By *Heinz Hoberg* and *Siegfried Krause*[*]

Although evidence for the occurrence of Al—Al bonds has been reported[1], there is no lack of critical observations casting doubt on the existence of this type of bond[2].

The stability of an Al—Al bond ought to be influenced by substituents having a +M or +I effect. Indeed, we have found that reaction (a)[3] (the dehalogenation of R(X)Al—Cl *(1)*, X = R^1_2N, R^1O, R = R^1 = *i*-C_4H_9, with alkali metals in apolar solvents *e.g.* hexane) involving deposition of Al does not take place, or if so only to a very limited extent. Instead, Al—Al units *(2)* are formed which, after filtration from accompanying alkali metal halide and unreacted alkali, can be identified by the formation of deuterium on solvolysis with CH_3OD [Equation (b)].

$$3R_2Al—Cl + 3M \rightarrow 2R_3Al + Al + 3MCl \quad (a)$$
(R = *n*-alkyl, aryl; M = alkali metal)



(1) *(2)*

$$\xrightarrow[-2\ Al(OCH_3)_3]{+6\ CH_3OD} D_2 + 2\ RD + 2\ XD \quad (b)$$

	R	X	D_2 formation [% amount calc. from Eq. (b)]
(a)	C_2H_5	CH_3O	0
(b)	*i*-C_4H_9	*i*-C_4H_9O	92
(c)	C_2H_5	$(CH_3)_2N$	0
(d)	*i*-C_4H_9	$(CH_3)_2N$	88
(e)	*i*-C_4H_9	*i*-C_4H_9	96

The +I effect of methyl groups in R and/or R^1 stabilizes the Al—Al group in *(2)*, as is shown by the formation of deuterium on solvolysis of *(2b)* and *(2d)*. "Stable" Al—Al units are also formed when exclusively *i*-C_4H_9 moieties are bonded to the aluminum. Thus, reaction of (*i*-$C_4H_9)_2$Al—Cl *(1e)* with potassium (1:1) leads to a product *(2e)* containing *ca.* 96% Al—Al units. Solvolysis with CH_3OD affords *i*-C_4H_9D and D_2 in the ratio 4:0.96 (calc. 4:1). Formation of a small amount of HD (*ca.* 4%) is probably due to the presence of Al—H or of CH_3OH in the CH_3OD.

A further indication that the *i*-C_4H_9 moieties in *(2e)* stabilize the Al—Al bond is provided by the fact that addition of $(C_2H_5)_3Al$ to a solution of *(2e)* (0.4 M in hexane) leads *via* alkyl exchange[4], to formation of unstable (C_2H_5)Al—Al units which undergo reaction with separation of Al. Deposition of Al does not take place on addition of (*i*-$C_4H_9)_3$Al.

Whether steric effects associated with the *i*-C_4H_9 moiety also contribute to the stability of the Al—Al bond is as yet undecided. The compounds *(2)* are diamagnetic and consequently are not present as R_2Al radicals[5]. They cannot be purified by distillation; on distillation of the dark-brown solution, monomeric triisobutylaluminum *(3e)* distils over at *ca.* 80 °C and 10^{-3} torr, apparently as a result of disproportionation. The remaining "polymeric" *(4)*[6] of unknown structure shows a Al:RD:D_2 ratio of 1.3:1.6:1 instead of 2:4:1 as for *(2e)*. It decomposes above *ca.* 130 °C to (*i*-$C_4H_9)_3$Al and aluminum.

$$n(i\text{-}C_4H_9)_2Al—Al(i\text{-}C_4H_9)_2 \rightarrow$$
(2e)
$$(n-1)(i\text{-}C_4H_9)_3Al +$$
(3e)
$$(i\text{-}C_4H_9)_2Al—(Al\text{-}i\text{-}C_4H_9)_{(n-1)}—Al(i\text{-}C_4H_9)_2$$
(4)

These results could also constitute confirmatory evidence for occurrence of the hitherto questionable Al—Al bond in the reaction of Al atoms with 2-butene[7].

Tetraisobutyldialuminum (2e)

1.6 g (40 mmol) potassium (pellets) is added to a solution of diisobutylaluminum chloride *(1e)* (7.0 g, 40 mmol) in hexane (100 ml) cooled to 0 °C and the mixture stirred vigorously for *ca.* 120 h. The KCl (2.9 g) which separates out is filtered off and solvent removed from the filtrate at 0 °C/12 torr. Residue: 5.6 g (viscous, brown), Al: calc. 19.1%, found 18.7%. Solvolysis: with 5 ml CH_3OD, 0.436 g residue affords 131.6 Nml *i*-C_4H_9D, 31.6 Nml D_2, and 2.3 Nml HD (determined mass spectrometrically).

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CAS Registry numbers:
(1a), 18890-76-1; *(1b)*, 2678-53-7; *(1c)*, 60253-65-8; *(1d)*, 60253-66-9; *(1e)*, 1779-25-5; *(2a)*, 60253-67-0; *(2b)*, 60253-68-1; *(2c)*, 60253-69-2; *(2d)*, 60253-70-5; *(2e)*, 60253-71-6

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[1] *E. P. Schram*, Inorg. Chem. *5*, 1291 (1966); *E. P. Schram*, R. E. Hall, and *J. D. Glore*, J. Am. Chem. Soc. *91*, 6645 (1969).
[2] *H. Nöth*, Prog. Boron Chem. *3*, 283 (1970).
[3] *K. Ziegler* and *H. Lehmkuhl* in *Houben-Weyl-Müller*: Methoden der organischen Chemie. 4th Edit. Thieme, Stuttgart 1970, Vol. 13/4, p. 51; *T. Mole* and *E. A. Jeffery*: Organoaluminum Compounds. Elsevier, Amsterdam 1972, p. 37.
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[7] *P. S. Skell* and *M. J. McGlinchey*, Angew. Chem. *87*, 215 (1975); Angew. Chem. Int. Ed. Engl. *14*, 195 (1975).

Nitrogen Transfer from a Diazoalkane to a Metal Center[1]

By *Manfred L. Ziegler, Klaus Weidenhammer, Hartmut Zeiner, Philip S. Skell,* and *Wolfgang A. Herrmann*[*]

Diazoalkanes are thermolytically, photolytically, or catalytically cleaved into carbenes and dinitrogen. While stable transition metal-carbene complexes can be prepared by means of such reactions, syntheses of organometallic derivatives of molecular nitrogen starting from diazoalkanes were hitherto unknown.

In investigations on the complex chemistry of halodiazoalkanes we have now observed halogen-free, nitrogen-containing coordination compounds: reaction of the tetrahydrofuran complexes $(\eta\text{-}RC_5H_4)Mn(CO)_2THF$ [*(1a)*, R=H; *(1b)*, $R=CH_3$] with 1,1,1-trifluorodiazoethane *(2)* at −80 to +25°C yields the diamagnetic dinitrogen complexes *(3a)* and *(3b)*, which can be separated from other products by column chromatography.

$[(\eta\text{-}C_5H_5)Mn(CO)_2]_2N_2$ *(3a)* $[(\eta\text{-}CH_3C_5H_4)Mn(CO)_2]_2N_2$ *(3b)*

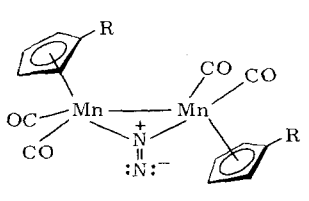
μ-Dinitrogen-bis(dicarbonyl-η-cyclopentadienylmanganese) *(3a)* and its derivative *(3b)* methylated in the C_5-ring are light-brown crystalline compounds which are air-stable for a brief period of time and are also thermally stable up to their decomposition temperatures (85 to 86°C and 73 to 74°C, resp.). Solutions in hydrocarbons or polar solvents (acetone, CH_2Cl_2) on the other hand, are extremely air-sensitive. We have characterized the compounds by elemental analysis, low- and high-resolution mass spectrometry, osmometric molecular weight determinations, and by ^{1}H-NMR and IR spectra (Table 1).

Table 1. Spectroscopic data of the dinitrogen complexes *(3a)* and *(3b)*.

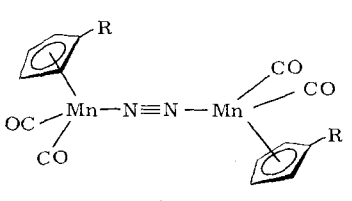
(3a): IR (*n*-pentane): 1975 m-s (ν_{N_2}), 1962 vs and 1918 vs (ν_{CO}).—^{1}H-NMR (100-MHz FT spectrum; C_6D_6; int. TMS): 6.10 ppm (singlet τC_5H_5).—MS (70 eV; T_Q 80°C; AEI MS-902): M^+ (*m/e* 380; rel. int. 100%); $(M-N_2)^+$ (352; <1); $(M-N_2-CO)^+$ (324; 11); $(M-N_2-2CO)^+$ (296; 12); $(M-N_2-3CO)^+$ (268; 40); $(M-N_2-4CO)^+$ (240; 18); $(C_5H_5)Mn(C_5H_6)^+$ (186; 30); $(C_5H_5)_2Mn^+$ (185; 41).

(3b): IR (*n*-pentane): 1971 m-s (ν_{N_2}), 1958 vs and 1913 vs (ν_{CO}).—^{1}H-NMR (100-MHz FT spectrum; C_6D_6; int. TMS: 6.19 and 8.50 ppm (AA'BB' center and singlet, resp., τC_5H_4 and τCH_3, resp.).—MS (70 eV; T_Q 60°C; AEI MS-902): M^+ (*m/e* 408; rel. int. 9%); $(M-N_2)^+$ (380; <1); $(M-N_2-CO)^+$ (352; 3); $(M-N_2-2CO)^+$ (324; 10); $(M-N_2-3CO)^+$ (296; 3); $(M-N_2-4CO)^+$ (268; 9); $(CH_3C_5H_4)_2Mn^+$ (213; 100).

The spectroscopic and analytical data are consistent with two isomeric structures *(A)* and *(B)* for *(3a)* and *(3b)* with *N,N*- and *N,N'*-coordinated dinitrogen, respectively. The linearly bridged isomer *(B)*, with R=H, has already been



(A)



(B)

described as a green compound that is unstable under normal conditions[2], and the IR spectrum was inconsistent with the presence of a centrosymmetric molecule. A complete three-dimensional X-ray structure analysis of *(3b)*[3], however, proved that *(3b)* belonged to the *N,N'*-coordinated type of compound *(B)* (Fig. 1): The N_2 ligand in the almost linear Mn—N≡N—Mn system [∢Mn,N,N = 176.5(4)°] has a N—N bond length of 111.8(7) pm. Crystallographically, *(3b)* has a center of symmetry (Z=2), the two cyclopentadienyl rings being *trans* to each other. The interplanar angle is 0°.

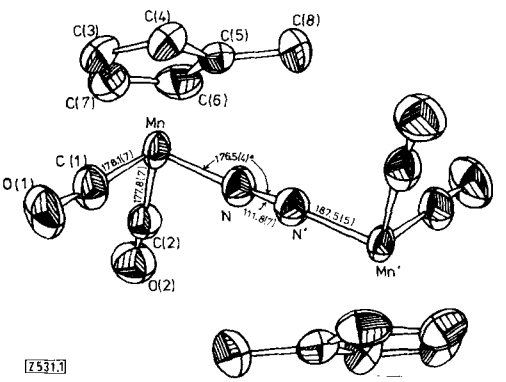


Fig. 1. ORTEP representation of molecule *(3b)*. The thermal ellipsoids correspond to the 50% probability surfaces; all atoms are drawn to scale (bond lengths in pm).

The preferred loss of N_2 from *(3a)* and *(3b)* in the mass spectrometer is unexpected for structure *(B)* and indicates a possible equilibrium between *(A)* and *(B)* in the ground state or in the M^+ state. A comparable initial cleavage of N_2 is known in the case of 1,3-substituted triazenes[4].

Thermal or catalytic cleavage of N_2 from *(2)* cannot be responsible for the formation of the dinitrogen complexes *(3a)* and *(3b)*: *(1a)* and *(1b)* react with N_2 at atmospheric pressure[5] and high pressure[6] to give the mononuclear complexes $(\eta\text{-}RC_5H_4)Mn(CO)_2N_2$[5] exclusively. Compounds *(3a)* and *(3b)* are therefore the result of a diazoalkane → metal complex nitrogen transfer. The experimental findings presented here do not suffice for a full interpretation of the mechanism, but it may be assumed that the terminal attack of the diazo function on the organometallic fragment $(\eta\text{-}RC_5H_4)Mn(CO)_2$ represents the primary step. That a primary end-on coordination of diazoalkanes is possible in the system mentioned here follows from isolation of a 1:1 complex which is thermally stable up to *ca.* 80°C on using diethyl diazomalonate instead of *(2)*[7]. The driving force for the elimination of the carbene substituents from the complexed diazoalkane is probably the intramolecular stabilization (by a 1,2 fluorine shift[8]). Also in accord with this postulate is the formation of *(3b)*, likewise observed on reaction with diazoethane [H instead of F in *(2)*], but absent on reaction with diazomethane[9].

The complete series N_2, $C_5H_5Mn(CO)_2N_2$[5], and μ-$N_2[C_5H_5Mn(CO)_2]_2$ makes it clear that the bond order of of dinitrogen expressed as a precentage lowering of the stretching vibration frequency decreases by comparable amounts in the first ($N_2 \rightarrow M—N_2$) and second ($M—N_2 \rightarrow M—N\equiv N—M$) complexation steps (6.9 and 8.9%, resp.):

	:N≡N:	M—N≡N:	M—N≡N—M
ν_{N_2} (cm^{-1})	2331	2169	1975

M = η-$C_5H_5Mn(CO)_2$

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Experimental:

A 0.5 M solution of *(2)*[11] in diethyl ether (10 ml) is added dropwise to a solution of $(\eta\text{-}RC_5H_4)Mn(CO)_2THF$ [*(1a)* or *(1b)*, resp.][10], prepared from $(\eta\text{-}C_5H_5)Mn(CO)_3$ (2.04 g, 10 mmol) or $(\eta\text{-}CH_3C_5H_4)Mn(CO)_3$ (2.18 g, 10 mmol), in THF (150 ml). On warming to room temperature the initially wine-red solution turns orange-yellow. After 3 h the solvent is evaporated in a vacuum, the residue extracted with *n*-pentane, and the extract purified by chromatography with *n*-pentane/benzene (2:1) on silica gel (Fischer Scientific Co, 100—200 mesh; $l=40$, $\phi=1.2$ cm; 10 °C). Recrystallization from *n*-pentane at −35 °C furnishes analytically pure *(3a)* or *(3b)*. Yield: 45 to 175 mg (not optimized).—*(3b)* is also isolated after reaction of *(1b)* with diazoethane, but is not formed with diazomethane[9] or diethyl diazomalonate[6].

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(1a), 12093-26-4; *(1b)*, 51922-84-0; *(2)*, 371-67-5; *(3a)*, 60270-10-2; *(3b)*, 60270-11-3

[1] Part 16 of the series: Complex Chemistry of Reactive Organic Compounds. This work was supported by the Deutsche Forschungsgemeinschaft and the US Air Force (Grant AFOSR 75—2748).—Part 15: *A. D. Redhouse* and *W. A. Herrmann*, Angew. Chem. *88*, 652 (1976); Angew. Chem. Int. Ed. Engl. *15*, 615 (1976).
[2] *D. Sellmann*, *A. Brandl*, and *R. Endell*, J. Organomet. Chem. *90*, 309 (1975); *D. Sellmann*, private communication, March 25, 1976.
[3] The compound crystallizes from pentane (−35 °C) monoclinically in the space group $C_{2h}^5-P2_1/n$ with $a=800.4(2)$, $b=1034.4(3)$, $c=1013.5(3)$ pm, $\beta=97.69(4)°$; $Z=2$. 1455 independent non-equivalent reflections were recorded with an automatic single-crystal diffractometer (AED, Siemens) and corrected in the usual way; $R=5.8$ %.
[4] *J. R. Plimner*, *P. C. Kearney*, *H. Chisaka*, *J. B. Yount*, and *U. I. Klingebiel*, J. Agric. Food Chem. *18*, 859 (1970).
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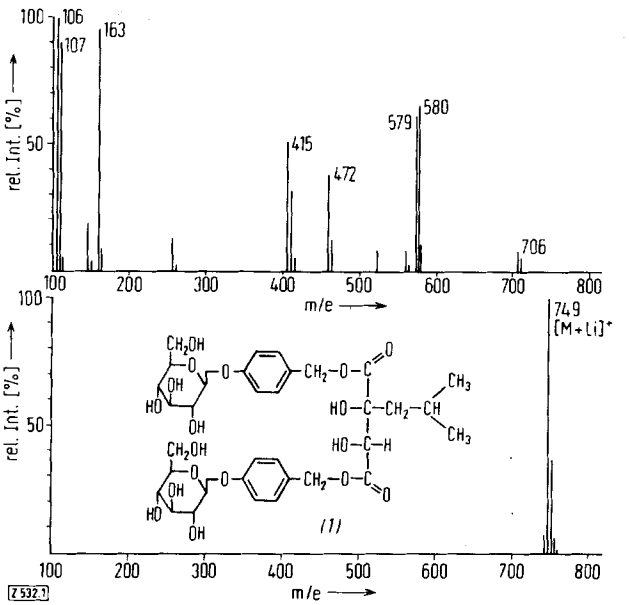
[11] *H. Gilman* and *R. G. Jones*, J. Am. Chem. Soc. *65*, 1458 (1943).

Li^+-Attachment—A Soft Ionization Method in Field Desorption Mass Spectrometry

By *Hans J. Veith*[*]

The molecular weights of non-volatile substances can be determined by means of field desorption mass spectrometry[1]. However, thermal and field-induced fragmentations frequently occur at the anode temperature necessary for the desorption of polar compounds. In the following it is shown that by Li^+-attachment[2] extraordinarily stable cluster ions $[M+Li]^+$[3] are formed which also permit the molecular weights of thermally sensitive substances to be determined.

$Li^+[CH_3B(C_6H_5)_3]^-$ or $Li^+[B(C_6H_5)_4]^-$ serve as Li^+ donors. The emitter filament is dipped into a saturated methanolic solution of the lithium salt and then heated for a short while at *ca.* 150 °C in a high vacuum. The substance under investigation is then applied to the emitter in the usual way[1]. Under these conditions the FD mass spectrum of sucrose ($M=342$) shows exclusively a quasi-molecular ion $[M+Li]^+$ at $m/e=349$. While in the normal FD spectrum of sucrose an $[M+1]^+$ ion occurs as base peak at $m/e=343$ within only a narrow temperature range and an increase in temperature effects immediate fragmentations, an increase in the heating current by more than 5 mA is necessary before the $[M+Li]^+$ ion is accompanied by the protonated molecular ion $[M+1]^+$ (relative intensity 3%) and fragment ions in the Li^+-attachment spectrum. Thus, Li^+-attachment permits differentiation between the M^+ and $[M+1]^+$ ions of unknown compounds. Moreover, the fragmentations are suppressed by the formation of the stable non-radical $[M+Li]^+$ ions, *i.e.* the mass spectrum contains only the signal for the quasi-molecular ion $[M+Li]^+$. Hence, it can be established whether the sample being analyzed is a mixture or a pure compound.



No peaks for the M^+ or $[M+1]^+$ ion are observed in the FD mass spectrum of the glucoside loroglossin *(1)*, $M=742$][4]. Apart from the fragmentations there is merely one additional line at $m/e=706$ for $[M-2H_2O]^+$ (Fig. 1, above). On the other hand the Li^+-attachment spectrum shows an intense signal for the quasi-molecular ion $[M+Li]^+$ at $m/e=749$ (Fig. 1, below). Hence, Li^+-attachment also facilitates generation of quasi-molecular ions of those substances whose normal FD spectrum contains no signals for the molecular ion.

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CAS Registry numbers:
(1), 60324-74-5

[1] *H. D. Beckey* and *H. R. Schulten*, Angew. Chem. *87*, 425 (1975); Angew. Chem. Int. Ed. Engl. *14*, 403 (1975).
[2] *F. W. Röllgen* and *H. R. Schulten*, Z. Naturforsch. *30a*, 1685 (1975); the method described by these authors for Li^+-attachment cannot be used generally in FD mass spectrometry.
[3] *F. W. Röllgen* and *H. R. Schulten*, Org. Mass Spectrom. *10*, 660 (1975).
[4] *R. W. Gray*, *A. Guggisberg*, *K. P. Segebarth*, *M. Hesse*, and *H. Schmid*, Helv. Chim. Acta *59*, 645 (1976).

$[(CH_3)_3SiNH]_2PN_3S_2$: An Unusual Dark Blue Sulfur-Nitrogen-Phosphorus Compound[1]

By *Rolf Appel* and *Mechthild Halstenberg*[*]

We have found that tetrasulfur tetranitride *(2)* also numbers among those sulfur-nitrogen compounds having SN multiple

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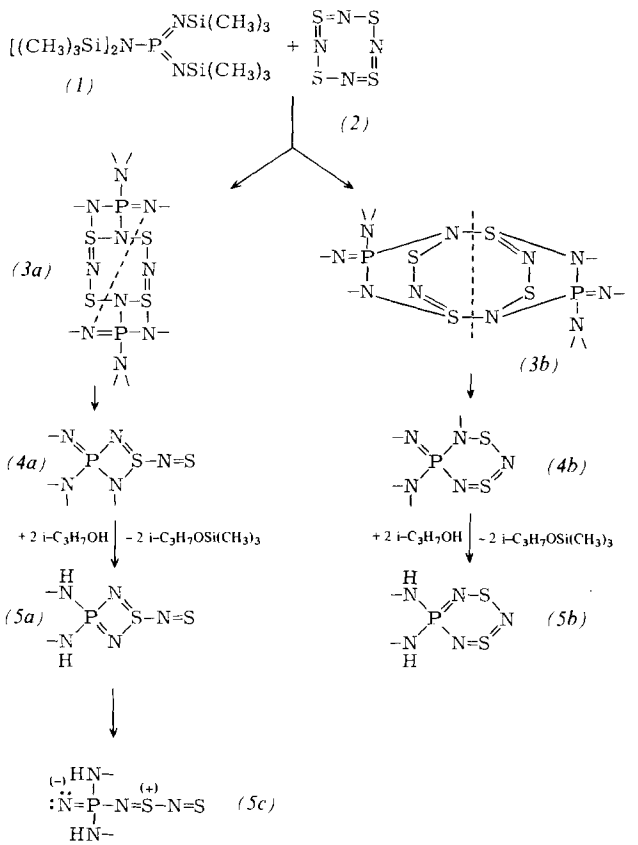
bonds which undergo cycloaddition with aminobis(imino)-phosphorane *(1)*[2, 3].

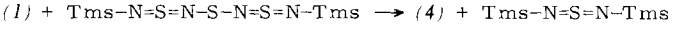
On addition of S_4N_4 to a solution of *(1)* in *n*-pentane (or benzene or ether) the solution turns dark red-brown, and an orange-yellow precipitate *(3)* appears which is shown by elemental analysis and molecular mass determination to be the diadduct of *(1)* to *(2)*, *i.e.* $S_4N_4 \cdot 2[Tms_2NP(NTms)_2]$ (Tms = trimethylsilyl).

The filtrate contains yet another homogeneous substance *(4)* of the same composition but having a molecular mass only half as large as the diadduct, which we therefore formulate as $S_2N_2 \cdot [Tms_2NP(NTms)_2]$. After removal of the solvent this brown-red substance can be purified by distillation. It crystallizes around room temperature and is extremely sensitive to hydrolysis. Even the slightest traces of moisture which creep through the grease sealing the ground glass joints of the apparatus lead to an intense blue color of the film of substance attached to the glass wall. On hydrolysis two silyl groups are eliminated as silyl ether. The same process can be accomplished by dissolution of the substance in isopropanol. Apart from isopropyl silyl ether the reaction yields a blue-violet compound *(5)* of composition $C_6H_{20}N_5PS_2Si_2$. This product, which is readily soluble in numerous solvents, crystallizes from *n*-pentane as dark blue-violet needles with a metallic sheen (m.p. 104 °C) closely resembling $KMnO_4$ crystals.



Concerning the reaction course and the structures of compounds *(3)*, *(4)*, and *(5)* we are still not able to decide between two possible suggestions which differ in the assumption of a 1,2- or a 1,4-cycloaddition to S_4N_4. In the case of 1,2-addition the tricyclic diadduct *(3a)* would contain two four-membered rings alongside the eight-membered ring of S_4N_4, while a 1,4-addition such as has recently been observed in the reaction of S_4N_4 with chlorosulfonyl isocyanate[4], would link up the P—N bonds of two molecules of *(1)* with one of *(2)* to from a tricyclic system *(3b)* consisting of an eight-membered ring and two six-membered rings.

Although the diadduct *(3)* can be isolated in rather poor yield it is unstable and decomposes symmetrically into the brown-red substance *(4)* of half the molecular mass for which the structure *(4a)* or *(4b)* comes into consideration. This compound, which is also accessible in good yield by heating of *(1)* with *N,N'*-bis(trimethylsilyl)trisulfur tetranitride *(6)*[5] according to



is stable in the absence of moisture. With proton-active compounds protonation takes place at two nitrogen atoms and two trimethylsilyl groups are eliminated. This reaction, which is accompanied by the impressive deepening of color, is shown by NMR studies to be accompanied by a proton exchange. It is impossible to decide between the four-membered ring structure *(5a)* or the six-membered ring structure *(5b)* for the dark-blue compound *(5)* only on the basis of the ^1H, ^{13}C, and ^{31}P-NMR data.

Both proposed structures *(5a)* and *(5b)* are supported by elemental analyses and molecular mass determinations. They also accord with the clear-cut formation reaction and NMR data. Predictably, the ^{31}P-NMR spectra of the compounds *(3)*, *(4)*, and *(5)* in C_6H_6 each contain only one singlet at $\delta = +6.0$, $+25.1$, and -1.5 ppm, respectively; owing to the ready decomposition of *(3)* into *(4)* the signal of the latter also appears at $+25.1$ ppm in the spectrum of *(3)*. The signals of the silyl protons (in C_6D_6) display the following chemical shifts: *(3)*, $\delta = -0.43$ and -0.52 ppm in the ratio 3:1; *(4)*, $\delta = -0.32$ and -0.39 ppm in the ratio 3:1; *(5)*, $\delta = -0.15$ ppm; a broad signal at $\delta = -2.5$ ppm is to be assigned to the NH protons.

The ^{13}C-NMR spectra (in C_6D_6) are informative. The spectrum of *(4)* recorded at 22.6 MHz contains three signals at $\delta = -2.8$ (s), -3.7 (d, $^3J_{PNSiC} = 4$ Hz), and -4.7 ppm (s), in the intensity ratios 1:1:2. At 15.08 MHz the signal at $\delta = -3.7$ ppm also appears as a doublet with the same coupling constant. The coupling takes place between the C atom of the silylimino group and the P atom; it is also observed with *(1)*. During the protonation of *(4)* to *(5)* occurring on alcoholysis the exocyclic silylimino group is transformed into a silylamino group, whereupon the coupling disappears. In PN compounds coupling with more distant atoms is observed primarily with double bond systems, being much weaker in the case of single bonds.

In its ^{13}C spectrum at 22.6 MHz compound *(5)* merely displays a singlet at $\delta = -1.2$. The intense dark blue-violet color of *(5)* ($\lambda_{max}^{isooctane} = 570$ nm, $\varepsilon_{max} = 1070 \times 10^3$ cm^2 mol^{-1}) might possibly be best interpreted with the aid of the terminal thionitroso group, which to our knowledge has not hitherto been observed. However, an unusual and rather unlikely feature of structure *(5a)* is the appearance of two double bonds in the four-membered ring since pπ-dπ double bonds lead to an increase in the bond angles at P and S. We therefore consider it more probable that the strained ring resulting from a 1,2-cycloaddition would open to give an open-chain structure such as *(5c)*. Further evidence against *(5a)* is provided by the mass spectrum of *(5)* in which the molecular signal appears as base peak, thus indicating *(5)* to be surprisingly stable.

An X-ray structure analysis already in progress should reveal the nature of the structure and bonding.

Procedure:

Compound *(1)* (7.32 g, 20.0 mmol) is dissolved in *n*-pentane (60 ml) and the stirred solution mixed with S_4N_4 (1.84 g, 10 mmol).

a) After 6 h the resulting *(3)* is filtered off [yield *ca.* 38 %, m.p. 140 °C (dec.)] and compound *(4)* vacuum-distilled [yield 49 %, b.p. 113 °C/10^{-3} torr].

b) After 6 h isopropanol (10 ml) is added and the mixture stirred for 3 h before evaporating to dryness. The residue is taken up twice in *n*-pentane (2 × 50 ml), filtered hot, and the filtrate cooled to −78 °C, whereupon compound *(5)* crystallizes [yield 37 %, m.p. 104 °C].

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(1), 52111-28-1; *(2)*, 39586-10-2; *(3a)*, 60363-68-0; *(3b)*, 60363-69-1; *(4a)*, 60363-70-4; *(4b)*, 60363-71-5; *(5a)*, 60363-72-6; *(5b)*, 60363-73-7; ^{31}P, 7723-14-0; ^{13}C, 14762-74-4

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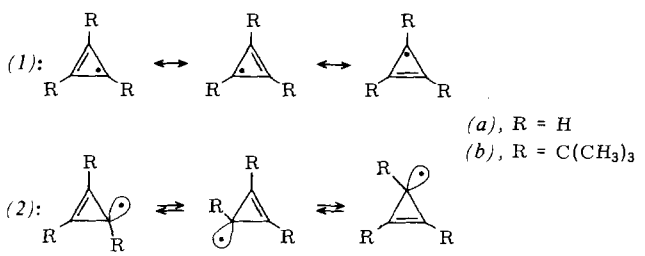
Electronic Structure of Tri-*tert*-butylcyclopropenyl[1]

By *Kurt Schreiner* and *Armin Berndt*[*]

Depending on the method of calculation employed a quantum mechanical examination of the electronic structure of the cyclopropenyl radical shows it to have aromatic, antiaromatic or σ character[2]. On irradiation of di-*tert*-butyl peroxide in cyclopropene a radical was obtained[3], whose *g*-factor with a value of 2.0061 lies outside the characteristic range (2.0025 ± 0.0005) for carbon radicals without heteroatoms. Even if the radical concerned is the desired cyclopropenyl radical, no decision could be made between the structures *(1a)* (aromatic π-radical) and *(2a)* (rapid equilibrium of energetically equivalent σ-radicals) on the basis of the observed proton coupling constants $a^H = 13.5$ G for three equivalent protons, since a^H values of *ca.* 10 G are expected for both radicals[4].



π- and σ-radicals can be distinguished unequivocally on the basis of their ^{13}C-ESR coupling constants, since the finite s character of the orbital of the unpaired electron in σ-radicals leads *via* direct Fermi contact to comparatively large a^C values. If, to a first approximation, it is assumed that the ring C-atoms of a cyclopropenyl radical have ^{13}C coupling constants similar to those of the comparable C-atoms of the vinyl radical ($a^C_\alpha = 107.57$, $a^C_\beta = -8.55$ G)[6] or 2,4,6-tri-*tert*-butylphenyl radical ($a^C_\alpha = 122.5$, $a^C_{ortho} = -6.16$ G)[7], then an a^C value of 30 to 37 G can be predicted for the ring C-atoms of *(2)* by weighted averaging (rapid equilibrium). On the other hand, the Karplus-Fraenkel expression[8] gives a a^C value of only *ca.* 4 G for the ring C-atoms of *(1)*.

With samples containing ^{13}C in natural abundance, ^{13}C-ESR coupling constants are conveniently accessible in the case of radicals kinetically stabilized by steric hindrance. We therefore carried out the reaction of tri-*tert*-butylcyclopropene with photochemically generated *tert*-butoxyl radicals in the ESR cell. Figure 1 shows the ESR spectrum (singlet) obtained at +55 °C in benzene together with the ^{13}C satellites occurring at higher amplification. The *g*-factor of 2.0026 and the number and relative intensities of the satellite signals are consistent with the constitution of a tri-*tert*-butylcyclopropenyl radical of structure *(1b)* or *(2b)*. From the intensities of the signals the coupling constant $a^C = 2.5$ G must be assigned to the nine methyl C-atoms; $a^C = 5.0$ G and $a^C = 30.0$ G then belong to the quarternary C-atoms of the *tert*-butyl groups and to the ring C-atoms, respectively.

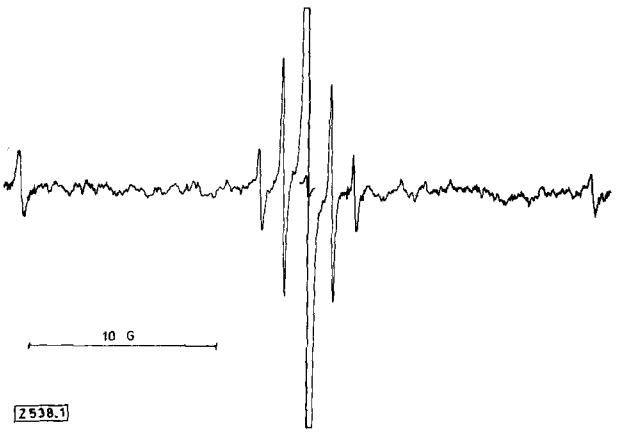


Fig. 1. ESR spectrum of the tri-*tert*-butylcyclopropenyl radical in benzene at +55 °C at low (small singlet in the middle) and high amplification. The difference in intensity of the outer satellite signals is due to decreasing radical concentration during the measurement.

Since from observations on other *tert*-butyl substituted π radicals, ^{13}C coupling constants of *ca.* 4 G each (as for the ring C-atoms) are to be expected for the methyl and quarternary C-atoms of the *tert*-butyl groups in *(1b)*, tri-*tert*-butylcyclopropenyl cannot have the electronic structure *(1b)*. The σ electronic structure *(2b)* is proven by the ^{13}C coupling constants of the ring C-atoms (30 G) lying within the predicted range.

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(1a), 60512-06-3; *(1b)*, 60512-07-4

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Lahnberge, D-3550 Marburg (Germany)

[1] Part 2 of the Electronic Structure of Cyclopropenyl Radicals. This work was supported by the Fonds der Chemischen Industrie and the Chemische Werke Hüls. Part 1: *K. Schreiner, W. Ahrens*, and *A. Berndt*, Angew. Chem. *87*, 589 (1975); Angew. Chem. Int. Ed. Engl. *14*, 550 (1975).
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[3] *G. Cirelli, F. Graf*, and *H. H. Günthard*, Chem. Phys. Lett. *28*, 494 (1974).
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[8] *M. Karplus* and *G. K. Fraenkel*, J. Chem. Phys. *39*, 1635 (1963).

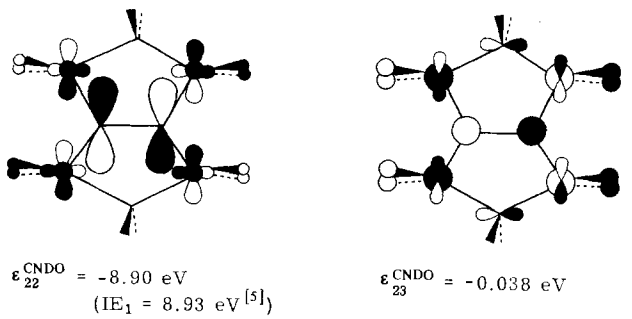
Radical Cation and Radical Anion of a Tetrasilyl-Substituted Ethylene[1, 2]

By *Hans Bock, Georg Brähler, Gerhard Fritz,* and *Eberhard Matern*[*]

Trimethylsilyl substituents have a differential effect on the individual molecular states of neighboring π systems: In general they act as π acceptors in radical anions[3a] or carbanions[3b], are weak donors in the ground state of the neutral compound[3c], and—as will be shown in the present communication—are able to considerably delocalize the positive charge in radical cations.

Experience shows[4] that radical cations $M^{\cdot\oplus}$ can be generated in solution from molecules M having first ionization energies $IE_1 \leq 8$ eV and characterized by ESR spectroscopy. Thus the first band in the photoelectron spectrum of the tetrasilyl-substituted ethylene derivative 2,2,4,4,6,6,8,8-octamethyl-2,4,6,8-tetrasilabicyclo[3.3.0]oct-1-ene[5] occurs at 7.98 eV, and the ESR spectrum of its radical cation is observed after reaction with $AlCl_3$ in CH_2Cl_2 at 180 K (Fig. 1).

A striking difference is observed in the ^{29}Si coupling constants $a^{\oplus}_{^{29}Si} = 22.71\ G \gg a^{\ominus}_{^{29}Si} = 6.72\ G$ (Fig. 1A): this is an interesting finding in view of the fact that double fixation of five-membered rings should lead to comparable geometries at the silicon sites of $M^{\cdot\oplus}$ and $M^{\cdot\ominus}$. CNDO calculations on the planar[7] parent compound 2,4,6,8-tetrasilabicyclo[3.3.0]oct-1-ene[5] show the inner orbitals to be:



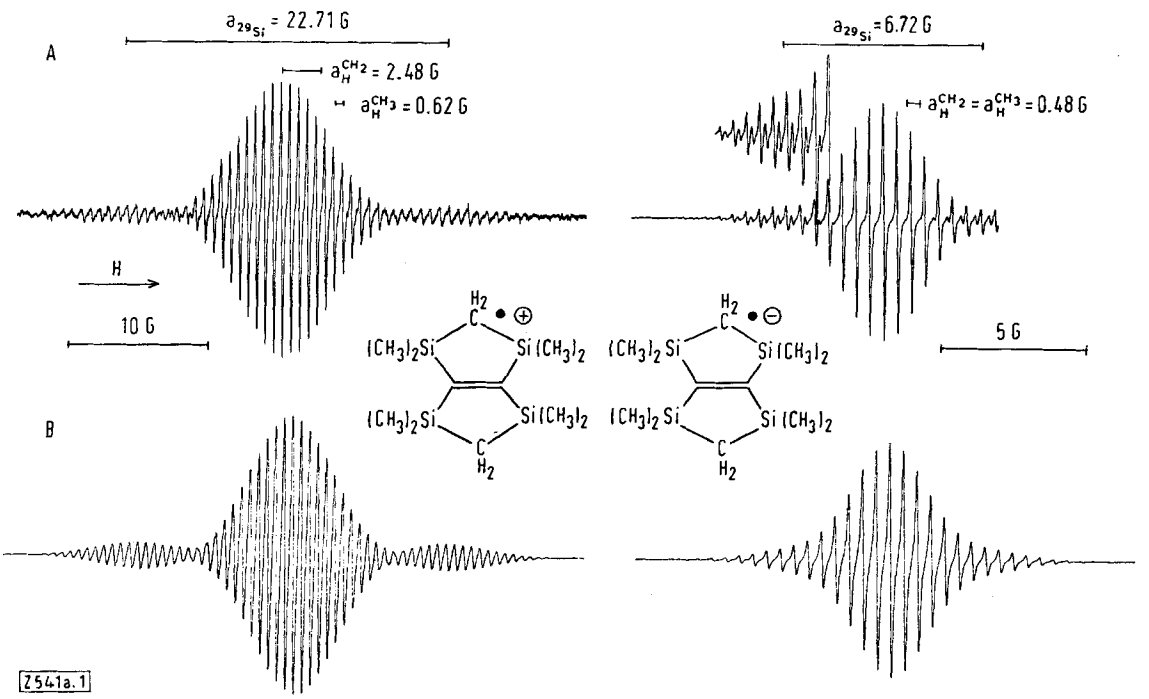


Fig. 1. Experimental (A) and simulated (B) ESR spectra of the radical cation and the radical anion of 2,2,4,4,6,6,8,8-octamethyl-2,4,6,8-tetrasilabicyclo[3.3.0]oct-1-ene.

The corresponding radical anion $M^{\cdot\ominus}$ can be generated with potassium in dimethoxyethane at 300 K; its ESR spectrum (Fig. 1) is only *ca.* 15 G wide and thus considerably narrower than that of the cation (*ca.* 35 G). The spectrum is expected to contain 25 signals for 24 methyl protons in the intensity ratio outermost line:central line = 1:2704156, a quintet for the four methylene protons, and a doublet for one ^{29}Si isotope per molecule (abundance 4.70 %, $I_{^{29}Si} = 1/2$). The ESR spectra were initially simulated without considering possible ^{13}C coupling and assuming degenerate constants $a_H^{CH_2} = n \times a_H^{CH_3}$[6] (Fig. 1B).

Bending by 30° along the C=C edge, *i.e.* ∢SiCSi = 122°, does not alter the type of orbital. Accordingly, the cation and the anion of the tetrasilyl-substituted ethylene should not represent π radicals but instead σ radicals and thus a new type of "persistent"[8] radical ion.

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CAS Registry numbers:
2,2,4,4,6,6,8,8-Octamethyl-2,4,6,8-tetrasilabicyclo[3.3.0]oct-1-ene radical cation, 60512-64-3; 2,2,4,4,6,6,8,8-octamethyl-2,4,6,8-tetrasilabicyclo[3.3.0]-oct-1-ene radical anion, 60562-10-9

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Englerstrasse 11, D-7500 Karlsruhe (Germany)

[1] Radical ions, Part 8.—Part 7: *F. Gerson, G. Plattner,* and *H. Bock*, Helv. Chim. Acta *53*, 1629 (1970).
[2] Cf. Lect. Abstr. 10th Organosilicon Symp., Windsor (Canada), April 3, 1976.

[3] a) Cf. *F. Gerson, J. Heinzer, H. Bock, H. Alt,* and *H. Seidl,* Helv. Chim. Acta *51*, 707 (1968), and references cited therein; b) *K. A. Ostoja Starzewski* and *H. Bock,* J. Am. Chem. Soc., in press; c) cf. *H. Bock* and *H. Seidl, ibid. 90,* 5694 (1968).
[4] *H. Bock, G. Brähler,* and *W. Kaim,* unpublished results.
[5] *G. Fritz, E. Matern, H. Bock,* and *G. Brähler,* Z. Anorg. Allg. Chem., in press.
[6] The ESIM program used was kindly provided by Prof. *V. Zelewsky,* Fribourg (Switzerland) and adapted to the Univac 1108 computer of Frankfurt University Computer Center by *W. Kaim.*
[7] *H. G. v. Schnering, E. Krahe,* and *G. Fritz,* Z. Anorg. Allg. Chem. *365*, 113 (1969).
[8] *D. Griller* and *K. U. Ingold,* Acc. Chem. Res. *9*, 13 (1976).

Radical Cations of Tetrasilyl-Substituted Hydrazines[1, 2]

By *Hans Bock, Wolfgang Kaim,* and *John W. Connolly*[*]

The radical anions of ethylene derivatives $R_2C{=}CR_2^{\bullet\ominus}$ are isoelectronic to the radical cations of similarly substituted hydrazines $R_2N{-}NR_2^{\bullet\oplus}$. In contrast to the isotope ^{12}C, however, ^{14}N has a nuclear spin and therefore provides ESR information ($I_{^{14}N}=1$) about the spin populations at the sites of the central bond. For these it follows only *indirectly* from comparison of the ^{29}Si coupling constants of tetrasilyl-substituted ethylene radical ions ($a^{\bullet\ominus}_{^{29}Si} \ll a^{\bullet\oplus}_{^{29}Si}$)[1,2] that they should be greater in the anion than in the corresponding cation.

Photoelectron spectra exhibit first ionization energies $IE_1 \leq 8$ eV for both bicyclic and open-chain tetrakis(trialkylsilyl)hydrazines. These compounds can accordingly be oxidized electrochemically and by $AlCl_3$, $AgBF_4$, or $SbCl_5$ in CH_2Cl_2 to the radical cations (Fig. 1), which are stable at room temperature in spite of their SiN bonds[3].

The ESR spectrum of the bicyclic derivative (Fig. 1) is dominated by the ^{14}N quintet; high resolution permits recognition of the more intense signals of the 25-line system of the 24 methyl protons, the quintet of the 4 methylene protons, and the doublet of one ^{29}Si isotope per molecule (abundance 4.70 %, $I_{^{29}Si}=1/2$). The ESR data are compared with those of tetraalkylhydrazines and of the isoelectronic ethylene radical anion in Table 1.

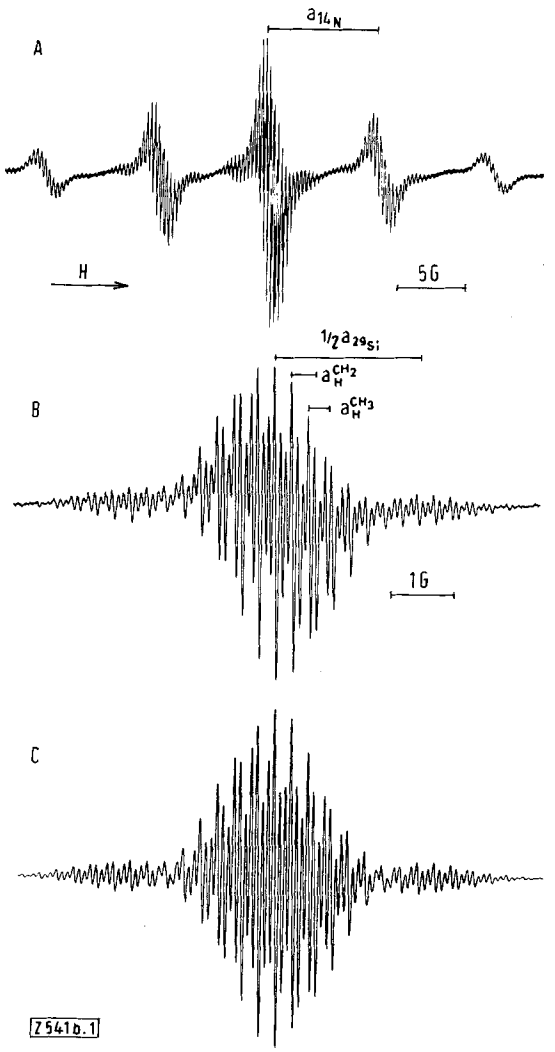
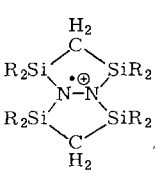
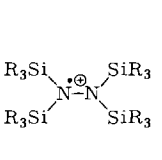
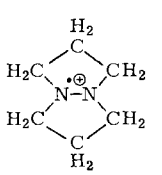
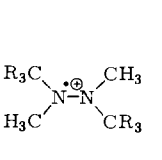
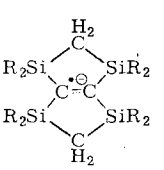


Fig. 1. Complete ESR spectrum (A), highly resolved central line (B) and its computer simulation (C) of the radical cation of 2,2,4,4,6,6,8,8-octamethyl-1,5-diaza-2,4,6,8-tetrasilabicyclo[3.3.0]octane (recording temperature: complete spectrum 300 K, section 240 K [4]).

Table 1. ESR coupling constants a_X [G] of tetrasilylhydrazine radical cations, tetraalkylhydrazine radical cations [4b], and tetrasilylethylene radical anion [1] (R = CH_3).

					
$a_{^{14}N}$	8.68	7.52	17.6	11.9	—
$a_H^{CH_2}$ (β)	—	—	15.6	11.9	—
(γ)	0.4 [a]	—	0.8	[b]	0.48
a_H^{β}	0.30	0.13	—	[b]	0.48
$a_{^{29}Si}$	5.00 [c]	[b]	—	—	6.7

[a] Temperature dependent (300 K: 0.38 G; 170 K: 0.43 G).
[b] Not observed.
[c] Temperature dependent (300 K: 5.00 G; 180 K: 5.30 G).

Comparison of the coupling constants reveals:

1) The difference between the ^{14}N coupling constants of bicyclic and open-chain hydrazine radical cations is considerably smaller for the tetrasilylated derivatives (1.2G) than for the tetraalkylated ones (cf. Table 1 and ref. [4b]). This can be interpreted by assuming that the bulky substituents

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extensively flatten the molecular skeleton around the nitrogen atoms and that the SiNSi angle (presumably near 120°) will therefore change less than the CNC angle.

2) The ^{14}N coupling constant of the tetrakis(trimethylsilyl)-hydrazine radical cation is at least 3 G smaller than that of analogous tetraalkyl derivatives[6] and equal to that of the tetraphenylhydrazine radical cation[5]. Thus trimethylsilyl and phenyl groups lower the spin density at the nitrogen atoms to the same extent.

3) The coupling constants of the bicyclic tetrasilylhydrazine radical cation differ considerably from those of the corresponding (nonmethylated)[6] tetraalkyl derivative, but are comparable with those of the isoelectronik tetrasilylethylene radical anion. In the latter system the larger coupling constants of the peripheral hydrogen atoms (Table 1: $a_H^{CH_2(\gamma)}$ and $a_H^{CH_3}$) and the larger $a_{^{29}Si}$ value[7] suggests a somewhat lower spin density in the central $>C=C<^{\ominus}$ bond relative to $>N-N<^{\oplus}$

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CAS Registry numbers:
Radical ions shown in the Table (from left to right): 60512-65-4; 60512-66-5; 60512-67-6; 60512-68-7; 60562-10-9

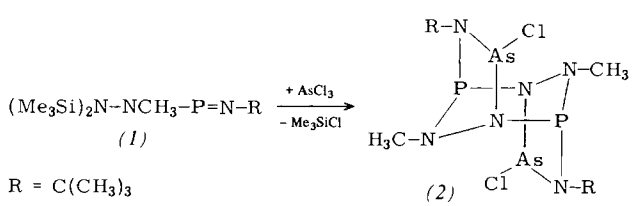
[1] Radical ions, Part 9.—Part 8: *H. Bock, G. Brähler, G. Fritz*, and *E. Matern*, Angew. Chem. *88*, 765 (1976); Angew. Chem. *15*, 699 (1976).
[2] Cf. Lect. Abstr. 10th Organosilicon Symp., Windsor (Canada), April 3, 1976.
[3] *D. Griller* and *K. U. Ingold*, Acc. Chem. Res. *9*, 13 (1976); cf. also *R. West* and *B. Bichlmeier*, J. Am. Chem. Soc. *95*, 7898 (1973).
[4] a) Strong anisotropic symmetrical and unsymmetrical line broadening is already observed at room temperature; b) cf., *e.g., S. F. Nelsen, G. R. Weisman, P. J. Hintz, D. Olp*, and *M. R. Fahey*, J. Am. Chem. Soc. *96*, 2916 (1974) and references cited therein.
[5] *F. A. Neugebauer* and *S. Bamberger*, Chem. Ber. *105*, 2058 (1972). The tetraphenylhydrazine radical cation shows $a_{^{14}N} = 7.52$ G.
[6] Comparison of the coupling constants given in [4b] for the radical cations $>N-N<^{\oplus}_{CH<}$ and $>N-N<^{\oplus}_{C(CH_3)<}$ leads to a correction of *ca.* 0.2 G per methyl group introduced.
[7] Concerning the transferability of the Q_{Si} parameters, cf. *F. Gerson, J. Heinzer*, and *H. Bock*, J. Mol. Phys. *18*, 464 (1970).

Synthesis and Structure of a Hexaazadiphosphadiarsatricyclodecane

By *Otto J. Scherer, Walter Glässel, Gottfried Huttner, Albin Frank*, and *Peter Friedrich*[*]

Hitherto, exclusively adamantane-type structures have been demonstrated or proposed for the wide class of substances derived from ten-membered heterocycles P_4X_6 with, for example, X = O, NR or CH_2. We report here on the first case of a structure of the tricyclodecane type *(2)*.

Compound *(2)* is formed on reacting 2-phospha-1-tetrazene *(1)*[1] with arsenic trichloride:



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Doz. Dr. G. Huttner, Dipl.-Chem. A. Frank, and Dipl.-Chem. P. Friedrich
Anorganisch-chemisches Institut der Technischen Universität
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The product[2], which can be purified by sublimation—or better by recrystallization from C_6H_6 or CCl_4—slowly decomposes above 110 °C. The compound is readily soluble in CH_2Cl_2 and $CHCl_3$ in the cold, and in C_6H_6, *n*-hexane, and CCl_4[3] on warming. In the mass spectrum the largest fragment detectable at 70 and at 17 eV is the half-molecule [17 eV: $m/e = 255$ (4 % $M/2^+$), 220 (100 % $M/2^+ - Cl$)]. The relative molecular mass found ebullioscopically (benzene) is 519.

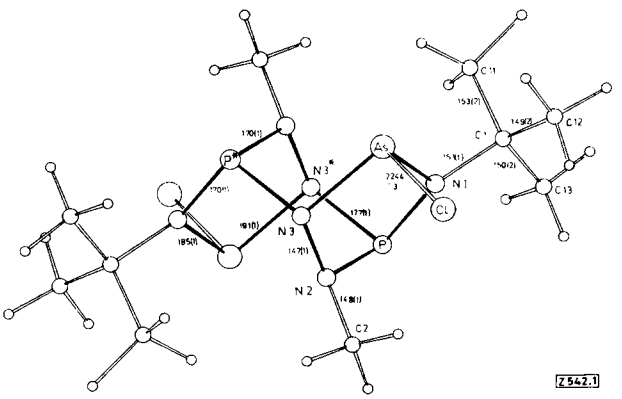

Fig. 1. Structure of *(2)*.

Figure 1 shows the results of an X-ray structure analysis[4]. *(2)* contains an inversion-symmetric (C_i symmetry) ten-membered polycycle [N3* and P* arise from N3 and P by inversion], which can be regarded as being made up of two identical five-membered rings As—N1—P—N2—N3. The As, N1, P, and N3 atoms lie to within 7 pm in a plane, which is at an angle of 41° to the N3, N2, P plane. The P—N bonds within the five-membered ring have a length of 170 pm and are shorter than the P—N3* bond coupling the two rings. The N—N, N—As, and As—Cl bond lengths correspond with those of single bonds[5].

Experimental:

A solution of $AsCl_3$ (5.9 g, 32.5 mmol) in ether (10 ml) is added dropwise to an ice-cold solution of *(1)* (9.0 g, 30.9 mmol) in ether (20 ml). The mixture is stirred for 1/2 h at room temperature and the apparatus evacuated under water-pump vacuum until the mixture becomes solid. The solid is taken up in 15 ml ether and the resulting solution stirred for 10 h, centrifuged, and the solvent removed under water-pump vacuum. The residue is then dissolved in 5 ml boiling benzene. On allowing to stand, crystals start to separate out after *ca.* 1 h. The residue of centrifugation is dried at 12 torr and recrystallized from 10 ml benzene. The combined crystals (3.27 g, 41 %) are recrystallized from hot benzene and washed with ice-cold CCl_4. Yield 1.95 g (25 %).

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German version: Angew. Chem. 88, 768 (1976)

CAS Registry numbers:
(1), 60385-03-7; *(2)*, 60385-04-8; $AsCl_3$, 7784-34-1

[1] For the preparation cf. *O. J. Scherer* and *W. Glässel*, Angew. Chem. *87*, 667 (1975); Angew. Chem. Int. Ed. Engl. *14*, 629 (1975).
[2] ^{31}P-NMR (20 % solution in $CHCl_3$, 85 % H_3PO_4 ext.): $\delta = -158.2$ ppm. ^1H-NMR (10 % solution in C_6H_6, TMS int.): $\delta CH_3C = -1.48$ (s), $\delta CH_3N = -2.68$ ppm (d), $^3J_{PH} = 16.2$ Hz.
[3] The phosphorus in *(2)* is obviously shielded in such a way that—in contrast to the violent oxidation that already takes place at room temperature in the case of most tris(amino)phosphanes—no reaction occurs even with warm CCl_4.
[4] Diffractometer SYNTEX-P 2_1, graphite monochromator, Mo-Kα, $\lambda = 71.069$ pm.—$C_{10}H_{24}As_2Cl_2N_6P_2$ *(2)*, monoclinic, space group $P2_1/c$, $a = 942$ (1), $b = 703$ (1), $c = 1631$ (1) pm, $\beta = 113.47°$, $Z = 2$. 737 independent diffraction intensities ($I \geq 3.1\,\sigma$) in the range $3 \leq 2\theta \leq 40°$, solution conventional, $R_1 = 0.051$. Structure resolving apparatus SYNTEX-XTL.—Para-

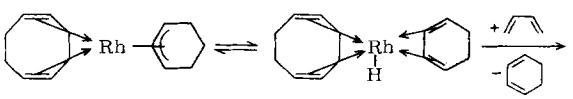
meters (atom/x:a/y:b/z:c): As / 0.1470(1) / 0.2149(2) / 0.0310(1)—P / 0.1331(4) / 0.6164(4) / −0.0271(2)—Cl / 0.3782(4) / 0.1713(5) / 0.1438(2)—N(1) / 0.202(1) / 0.396(1) / −0.0338(6)—N(2) / 0.1313(9) / 0.591(1) / 0.0766(5)—N(3) / 0.070(1) / 0.406(1) / 0.0852(5)—C(1) / 0.242(1) / 0.332(2) / −0.1117(7)—C(11) / 0.088(2) / 0.269(3) / −0.1896(9)—C(12) / 0.354(2) / 0.172(2) / −0.0811(9)—C(13) / 0.308(2) / 0.500(3) / −0.1421(9)—C(2) / 0.272(1) / 0.645(2) / 0.1559(8).

[5] *J. Weiss* and *W. Eisenhuth*, Z. Naturforsch. *22b*, 454 (1967); *R. Ullmann* and *H. Nöth*, Chem. Ber. *109*, 2581 (1976); literature cited therein.

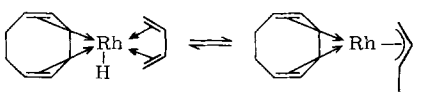
Cyclohexenyl(1,5-cyclooctadiene)iridium—η-Diene Hydride or Enyl Structure[**]

By *Jörn Müller*, *Walter Holzinger*, and *Helmut Menig*[*]

The transfer of a hydrogen atom from an η-enyl- or η-dienyl ligand to the central metal atom should play an important role in numerous reactions of π-complexes with olefins, *e.g.* ligand-exchange processes which are partial steps of catalytic isomerizations and oligomerizations of alkenes and dienes. Thus the ligand exchange[1] in the reaction of cyclohexenyl(1,5-cyclooctadiene)rhodium *(1)*[2] with butadiene may perhaps be most simply explained in terms of the formation of hydride intermediates [*(1a)*, *(1b)*].

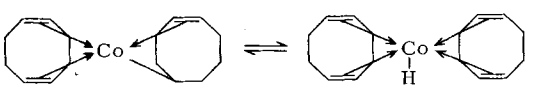


(1) *(1a)*



(1b)

Similarly the reactive behavior of 1,5-cyclooctadiene(4-5-η-cyclooctenyl)cobalt *(2)* suggests that this complex is in equilibrium with a hydride form *(2a)*[3].

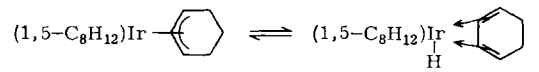


(2) *(2a)*

So far, however, there has been no direct spectroscopic evidence for an equilibrium of the type *(1)*⇌*(1a)* or *(2)*⇌*(2a)*.

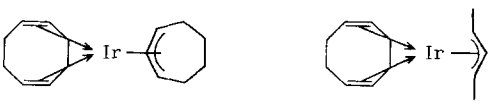
We have now synthesized and investigated the analog of *(1)*, the iridium compound *(3)*. Reaction under UV radiation of di-μ-chlorobis[(1,5-cyclooctadiene)iridium] *(4)*[4] with 1,3-cyclohexadiene in the presence of i-C_3H_7MgBr furnished *(3)* in the form of yellow-brown crystals. Spectroscopic findings prove that *(3)* is in equilibrium with a hydride form at room temperature, and that the six-membered ring ligand has a fluxional structure.

Evidence for the existence of an Ir—H bond is provided by the occurrence of a medium-strength absorption at 2010 cm^{-1} in the IR spectrum (KBr) and a broad singlet at $\tau = 12.6$ in the ^{1}H-NMR spectrum ([D_8]toluene). The protons of the cyclohexadiene ligand likewise give rise to only one singlet at $\tau = 6.76$. Both singlets become sharper on warming the solution; on cooling they broaden and at *ca.* 280 K disappear into the background. Accordingly, there must be rapid interchange between the forms *(3a)* and *(3b)*; collapse of the proton signal of the cyclohexadiene ligands comes about because hydride addition and abstraction, respectively, can take place at both sides of the π-system, so that this "rotates" over all six ring positions.



(3a) *(3b)*

On lowering the temperature the equilibrium shifts in favor of *(3a)*. This is confirmed by the temperature-dependence of the ^{13}C-NMR spectrum[5]. Cycloheptenyl(1,5-cyclooctadiene)iridium *(5)*, obtained by reaction of *(4)* with 1,3-cycloheptadiene in the presence of i-C_3H_7MgBr, behaves in exactly the same way as *(3)*. On the other hand, the 1,5-cyclooctadiene(pentenyl)iridium *(6)*, synthesized in a similar way, has so far yielded no evidence of a hydride form.



(5) *(6)*

Experimental:

All work must be carried out under nitrogen or argon. 1,3-Cyclohexadiene (2 ml) is added to a suspension of *(4)* (1.62 g, 2.41 mmol) in ether (20 ml) at −78 °C; a Grignard solution prepared from Mg (182 mg, 7.49 mmol) and i-C_3H_7Br (0.7 ml) in ether (30 ml) is then added with vigorous stirring. The mixture is allowed to warm slowly to 20 °C and irradiated for 5 h with UV light (Hg high-pressure lamp Q 81, Heraeus, Hanau). Solvent and excess diene are then removed by evaporation, the residue eluted with hexane (150 ml), and the resulting solution concentrated and chromatographed on an Al_2O_3 (5 % H_2O) column (length 50 cm, diameter 1.5 cm) with hexane. Analytically pure *(3)* crystallizes from the yellow-brown eluate at −78 °C. Yield 1.09 g (2.86 mmol; 59 %), m.p. 68—69 °C.

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German version: Angew. Chem. *88*, 768 (1976)

CAS Registry numbers:
(3a), 60410-67-5; *(3b)*, 60140-68-6; *(4)*, 12112-67-3; *(5)*, 60410-69-7; *(6)*, 60410-70-0

[1] *H.-O. Stühler*, Dissertation, Technische Universität München 1976.
[2] *J. Müller*, *H.-O. Stühler*, and *W. Goll*, Chem. Ber. *108*, 1074 (1975).
[3] *H. Bönnemann*, Angew. Chem. *85*, 1024 (1973); Angew. Chem. Int. Ed. Engl. *12*, 964 (1973).
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Simplified Synthesis of Bis(triphenylphosphoranylidene)methane

By *Rolf Appel*, *Fritz Knoll*, *Heinfried Schöler*, and *Horst-Dieter Wihler*[*]

Hexaorganylcarbodiphosphoranes of type $R_3P{=}C{=}PR_3$ are extremely reactive compounds[1-3] which on account of their pronounced ylide character avidly abstract protons and halogen[4]. Their wide-spread use, however, has hitherto been

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thwarted by the effort involved in their preparation. The reaction of triphenylphosphane with tetrachloromethane in polar solvents[5] recently described by us affords convenient entry to the bis(triphenylphosphoranylidene)methane *(2)*. [Chloro(triphenylphosphoranylidene)methyl]triphenylphosphonium chloride *(1)* and dichlorotriphenylphosphorane are formed in quantitative yield.

$$3\ Ph_3P + CCl_4 \longrightarrow \left[Ph_3P{=}C(Cl){=}PPh_3\right]^+ Cl^- + Ph_3PCl_2$$

(1)

We have now found that *(1)* can be readily dechlorinated to *(2)* by reaction with tris(dimethylamino)phosphane.

$$(1) + P[N(CH_3)_2]_3 \longrightarrow Ph_3P{=}C{=}PPh_3 + PCl_2[N(CH_3)_2]_3$$

(2)

Attempts to prepare the particularly reactive hexamethylcarbodiphosphorane[3] analog by dechlorination of [chloro(trimethylphosphoranylidene)methyl]trimethylphosphonium chloride *(3)*, now readily accessible from trimethylphosphane and CCl_4, were not as successful as had been hoped[6]. Dechlorination of *(3)* does in fact take place, but bis(trimethylphosphoranylidene)methane proves to be such an extremely strong base[3], which abstracts hydrogen chloride from dichlorotris(dimethylamino)phosphorane, so that only [(trimethylphosphoranylidene)methyl]trimethylphosphonium chloride *(4)* is found.

$$\left[(CH_3)_3P{=}C(Cl){=}P(CH_3)_3\right]^+ Cl^- \xrightarrow{P[N(CH_3)_2]_3} \left[(CH_3)_3P{=}CH{=}P(CH_3)_3\right]^+ Cl^-$$

(3) *(4)*

Experimental:

The reaction is carried out in a 250 ml round-bottomed flask fitted with side-tap and return frit which has previously been baked out and purged with argon. A mixture of *(1)* (40.0 g, 0.066 mol) and tris(dimethylamino)phosphane (10.8 g, 0.066 mol) is stirred in 150 ml benzene. Only a small amount of *(1)* dissolves and the suspension slowly turns yellow. After 24 hours the mixture is brought as quickly as possible to boiling (preheated oil-bath) and immediately filtered through the return frit. On cooling, *(2)* crystallizes from the already turbid filtrate. *(2)* is filtered off, washed twice with diethyl ether, and finally dried in a vacuum at room temperature. Yield 21.8 g (61%); m.p. 213—215 °C, literature[1]: 208—210 °C.

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CAS Registry numbers:
(1), 58513-97-6; *(2)*, 7533-52-0; tris(dimethylamino)phosphane, 1608-26-0

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Determination of the Absolute Configuration of Chiral Thiols by ^{1}H-NMR Spectroscopy of Diastereomeric Thiol Esters[**]

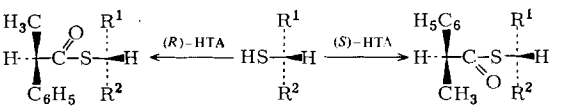
By *Günter Helmchen* and *Roland Schmierer*[*]

Dedicated to Professor Vladimir Prelog on the occasion of his 70th birthday

Several simple methods for determining the absolute configuration and enantiomeric purity of chiral alcohols and amines have already been reported[1]. The lack of corresponding methods for thiols has hitherto considerably hindered stereochemical and mechanistic studies on this class of substances[2]. We have now found that diastereomeric thiol esters of hydratropic acid (HTA) and other α-substituted phenylacetic acids differ significantly in their ^{1}H-NMR spectra. The relative configuration of the thiol esters and—since the absolute configuration of HTA is known[3]—the absolute configuration of the thiols can be determined in a simple way from the signs of the differences in the signal positions of constitutionally equivalent protons. In many cases it is also possible to determine the composition of mixtures of diastereomers, and thus the entiomeric purity of the thiols, on the basis of their NMR spectra or by gas chromatography.

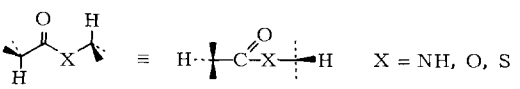
Our method can be summerized as a *rule*: A chiral thiol $HSCHR^1R^2$ possesses the absolute configuration *(1)*, if the signal of group R^1 of thiol ester *(2)* appears further downfield than the signal of group R^1 of thiol ester *(3)*, and/or the signal of group R^2 of thiol ester *(2)* appears further upfield than the signal of group R^2 of thiol ester *(3)*.

The rule is based on two arguments:



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

1. Data from the literature as well as a comparison of the ^{1}H-NMR spectra of analogous amides, esters, and thiol esters of α-alkylphenylacetic acids show that these compounds have an approximately planar basic structure *(4)*. Diastereomeric HTA thiol esters derived from the same thiol accordingly have the conformations *(2)* and *(3)*.



(4)

2. The different positions of the signals of the diastereotopic groups R^1 and R^2 result from a different shielding effect (up-field shift) of the phenyl group. The shielding effect on the group R^2 is stronger in *(2)* ("cisoid" arrangement of R^2 and phenyl) than in *(3)* ("transoid" arrangement of R^2 and phenyl). The converse applies for R^1.

The rule was checked experimentally on the compounds of known absolute configuration[4] listed in Table 1. Further confirmation follows from the fact that extensive agreement exists with analogous amides and esters, for which a corre-

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Table 1. ^{1}H-NMR signals [a] of thiol esters *(2)* and *(3)*.

		(2) δ [ppm] in		*(3)* δ [ppm] in	
		$CDCl_3$	C_6D_6	$CDCl_3$	C_6D_6
(a)	α	1.24	1.16	1.19	1.07
	β	0.874	0.863	0.848	0.839
	γ	1.203	1.080	1.266	1.186
(b)	α	0.877	0.818	0.790	0.698
	β	0.830	0.935	0.657	0.748
	γ	0.783	0.650	0.856	0.782
	δ		1.806		1.988
(c)	α	4.791	4.907	4.546	4.666
	β	4.617	4.740	4.441	4.559
	γ	1.723	1.775	1.574	1.628
	δ	0.811	0.632	0.879	0.742

[a] Bruker HX-90-E (PFT, 25°C, 0.1 M solution, TMS as internal standard).
[b] Quasi-singlet of half-width 7 Hz.
[c] Signal assignment of the methyl groups based on decoupling experiments and solvent effects.
[d] Almost centrally symmetric multiplet; α: 6 lines with distances >1 Hz, β: 8 lines with distances <1 Hz.

sponding rule has been confirmed without exception on more than 30 diastereomeric pairs.

Experimental:

A solution of 1 mmol thiol and 3 mmol 2-phenylpropionyl chloride in 5 ml carbon tetrachloride through which nitrogen is allowed to bubble is warmed to 50—60°C, until thin-layer chromatograms indicate that the desired conversion has taken place (1—3 days). For decomposition of the excess acyl chloride the mixture is concentrated *in vacuo* and the residue stirred for *ca.* 2 h with 2 ml dioxane/water (1:1). The solution is taken up in ether/benzene (7:3) and this is extracted with 1 N NaOH and water, dried and evaporated down. The thiol esters which are obtained in 80—90% yield are purified, if necessary, by preparative thin layer or column chromatography (UV absorption at 254 nm).

Enantiomerically pure 2-phenylpropionyl chloride is obtained by reaction of optically pure HTA[3] (3 mmol) with oxalyl chloride (2 ml) for 5 min at room temperature. The solution is subsequently concentrated *in vacuo* and the residue is taken up in 0.5 ml of dry benzene and evaporated down. This is repeated twice. Distillation of the product or addition of tertiary amines leads to partial racemization.

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CAS Registry numbers:
(1a), 50764-49-3; *(1b)*, 53273-24-8; *(1c)*, 60661-87-2; *(2a)*, 60661-88-2; *(2b)*, 60661-89-4; *(2c)*, 60661-90-7; *(3a)*, 60661-91-8; *(3b)*, 60661-92-9; *(3c)*, 60661-93-0; (*R*)-2-phenylpropionyl chloride, 36240-11-6; (*S*)-2-phenylpropionyl chloride, 25145-43-1

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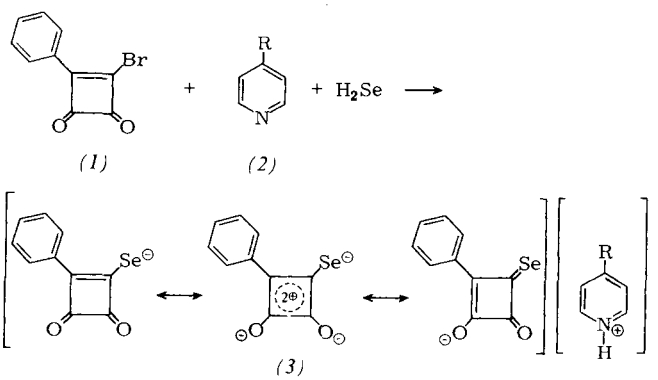
[3] *K. Petersen*, Ark. Kemi *10*, 283 (1956).
[4] All new compounds give correct elemental analyses. The thiols were prepared by reaction of tosylates of the corresponding alcohols with alkali metal xanthates.

Bond-Delocalized Cyclobuteneselenones

By *Arthur H. Schmidt, Walter Ried*, and *Peter Pustoslemsek*[*]

Organoselenium compounds have recently attracted considerable attention, with representatives having delocalized bonds commanding particular theoretical interest[1]. We now wish to present the first report of cyclobutenes having delocalized bond systems which incorporate selenium as substituent.

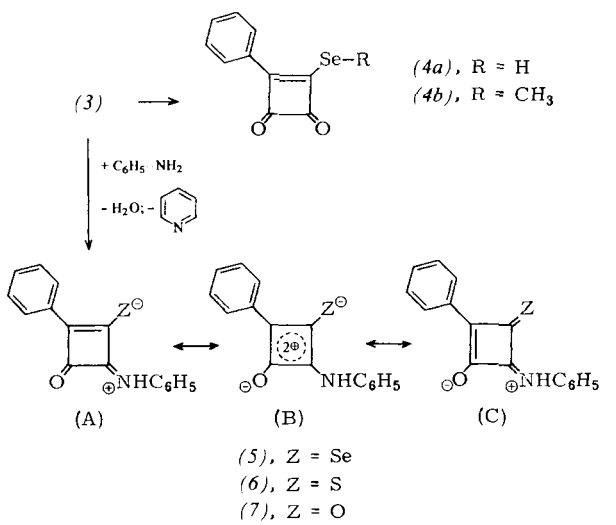
Dropwise addition of benzene solutions of *(1)* to pyridines *(2)* saturated with anhydrous hydrogen selenide[2] affords good yields of the pyridinium salts *(3)*. They are dark in color and are stable in the crystalline and dissolved states. Deposition of metallic selenium occurs only on prolonged heating of a solution in ethanol, especially in the presence of atmospheric oxygen. The IR spectra of the pyridinium 3-phenyl-4-selenatocyclobutenediylium-1,2-diolates *(3)* (Table 1) accord with the proposed salt structure.



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

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

Addition of the pyridinium salt *(3a)* or *(3b)* to 6 N hydrochloric acid yields 3-hydroseleno-4-phenyl-3-cyclobutene-1,2-dione *(4a)* as a yellow powder. Its structure was established by reaction with methyl iodide to give *(4b)*, which also arises on treatment of *(3a)* or *(3b)* with methyl iodide.



(4a), R = H
(4b), R = CH_3

(A) (B) (C)

(5), Z = Se
(6), Z = S
(7), Z = O

In keeping with its electrophilic character the four-membered ring system of the pyridinium salts *(3)* is readily attacked by nucleophilic reagents. Thus heating of equimolar solu-

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Table 1. Properties of compounds *(3a)*, *(4a)*, and *(5)* to *(7)*.

Cpd.	M.p. [°C] Solvent Color	IR [cm^{-1}]	UV λ_{max} [nm] (ε)	Ref.
(3a)	144—146 ethanol red	3200—2400 br, 1780 sh, 1740 s, 1720 s, 1520 m	in ethanol 383 (9060), 328 (18100), 268 (sh; 12900), 260 (sh; 14500), 254 (sh: 15800), 247 (16500), 202 (20050)	
(4a)	72—80 (dec.) yellow	3400—2400 br, 1775 s, br, 1755 s, br, 1635 w, 1590 w, 1525 w, 1465 w, 1380 m, 1230 s		
(5)	160 (dec.) acetonitrile brown	1770 w, 1740 s, 1635 m, 1580 m	in methanol 475 (1950), 347 (25100), 285 (9100), 233 (19300), 202 (23400)	
(6)	212—215 ethanol red	3165—2850 br, 1780 w, 1735 s, 1705 sh, 1650 w, 1590 w	in methanol 442 (2690), 327 (23200), 283 (12500), 229 (16500), 202 (20100)	[3]
(7)	275 (dec.) DMF yellow	3200—2600 br, 1780 w, 1660—1580 br	in methanol 393 (5150), 282 (sh; 15550), 268 (sh; 19500), 257 (21300), 215 (13800), 202 (20200)	[4]

tions of *(3a)* and aniline (THF/ethanol) with careful exclusion of atmospheric oxygen furnishes the condensation product *(5)*. Its structure was determined by spectroscopy (Table 1) and from analogies with the sulfur compound *(6)*[3].

Table 1 reveals considerable differences in the physical properties of the four-membered ring systems *(5)*, *(6)*, and *(7)* belonging to the same class of compounds. This finding indicates that the resonance structures (A) to (C) must be ascribed different weights, depending upon their substituent Z, in describing the ground state of compounds *(5)* to *(7)*. According to the IR spectrum, bond delocalization as implied by the resonance form (B) should be significant for compound *(7)* but not for *(5)* and *(6)*.

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CAS Registry numbers:
(1), 22315-46-4; *(2a)*, 110-86-1; *(2b)*, 108-89-4; *(3a)*, 60538-55-8; *(3b)*, 60538-56-9; *(4a)*, 60538-54-7; *(4b)*, 60538-57-0; *(5)*, 60553-54-0; *(6)*, 57652-47-8; *(7)*, 60553-55-1; SeH_2, 7783-07-5

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[4] *W. Ried*, *W. Kunkel*, and *G. Isenbruck*, Chem. Ber. *102*, 2688 (1969).

Electron Impact Induced Ether Cleavage by Anchimeric Participation of Silyl and Germyl Groups[1][**]

By *Helmut Schwarz* and *Manfred T. Reetz*[*]

Electron impact induced cleavages of O—C bonds with elimination of radicals and charge localization on the oxygen function require considerable energy and therefore afford intense fragment ions only in exceptional cases[2]. We recently found that (silyl)methyl alkyl ethers of type *(1a)* rearrange *via* rupture of the O—C bond to form *(3)* in the mass spectrometer[1]. Further investigations have now shown that this *new* kind of electron impact induced ether cleavage always occurs when the transition state *(2)* is stabilized by anchimeric participation[3] of $X(CH_3)_3$ groups (X = Si, Ge).

As shown by Table 1, the fragment ions relevant to our discussion are generated with widely varying intensities, depending upon the structure of the molecular ions. While the elimination of $X(CH_3)_3$ as radicals and also the formation of $[X(CH_3)_3]^+$ and $[R]^+$ can be explained by conventional rules of mass spectrometry (influence of activation energy and/or frequency factor), a complex mechanism must be assumed to account for cleavage of the O—R bond with generation of $[M-R]^+$ ion.

The hypothesis that this process could be a simple α cleavage is ruled out by the following experimental data: In the 13-eV spectra, usually dominated by processes of *lowest* activation energy, the $[M-R]^+$ ions from *all* compounds except *(1g)* are by far the most intense fragments (contribution to total ion current >83%), whereas, for example, formation of $[X(CH_3)_3]^+$ by dissociation of the relatively weak C—Si and C—Ge bond is strongly suppressed. Since genesis of $[M-R]^+$ fails to occur in the case of the *tert*-butyl derivative *(1g)*, in spite of the possibility of eliminating a low-energy benzyl radical, it must be assumed that the energy balance of ether cleavage in the silyl and germyl compounds *(1a)* to *(1f)* is considerably improved by *simultaneous* intramolecular bonding. A model can be seen in the neighboring group participation of silyl and germyl groups, in which coordination in the transition state *(2)* due to d orbitals weakens the O—R bond and thus permits rearrangement to the oxonium ion *(3)*. The absence of $[M-R]^+$ ions in the case of *(1g)* supports the decisive role of the silyl and germyl groups and shows that the generation of oxonium ions by an alternative migration of the C^9—C^{10} σ bond of the fluorenyl system to the oxygen, which is accompanied by ring expansion, cannot compete with silyl and germyl migration[4]. The observation that hydrogen scrambling processes—which are otherwise

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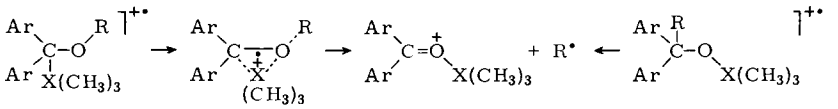


(1) (2) (3) (4)

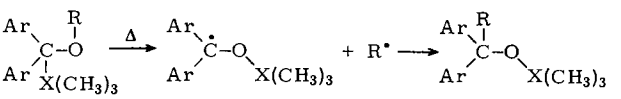
Ar + Ar = 2,2'-biphenylylene

Table 1. Selected lines from the mass spectra of the molecular ions *(1a)* to *(1g)* and *(4a)* and *(4b)* [a].

Cpd.	M	Fragment Ion R	$[M-X(CH_3)_3]^+$ 70 eV	$[M-X(CH_3)_3]^+$ 13 eV	$[M-R]^+$ 70 eV	$[M-R]^+$ 13 eV	$[X(CH_3)_3]^+$ 70 eV	$[X(CH_3)_3]^+$ 13 eV	$[R]^+$ 70 eV	$[R]^+$ 13 eV
(1a)	Si	$CH_2C_6H_5$	0.1	—	31.0	93.6	43.7	0.8	10.9	0.1
(1b)	Si	$CH_2CH=CH_2$		—	16.9	93.5	58.9	5.0	6.3	–
(1c)	Si	$CD_2CH=CH_2$	—	—	16.7	92.8	58.4	5.3	6.2	
(1d)	Ge	$CH_2C_6H_5$	0.1	—	20.5	93.9	48.1	4.9	21.0	1.4
(1e)	Ge	$CH_2CH=CH_2$	0.1	—	15.4	83.1	46.9	6.5	7.6	0.1
(1f)	Ge	$CD_2CH=CH_2$	0.1	—	15.6	83.3	46.4	6.7	7.5	
(1g)	C	$CH_2C_6H_5$	13.0	64.8	0.1	0.1	4.6	0.1	64.9	1.9
(4a)	Si	$CH_2C_6H_5$	< 0.1	0.2	46.3	93.6	37.9	0.8	2.3	< 0.1
(4b)	Si	$CH_2CH=CH_2$	—	—	28.5	94.4	42.7	2.1	0.6	–

[a] The percentage intensities are based on $\%\Sigma_{40}$, including the contributions of all isotopes of Ge and Si. All data are average values of at least four measurements. The ionization energies correspond to the nominal values. Experimental conditions: CH 7 mass spectrometer (Varian MAT); emitter current 300 and 100 μA, respectively; temperature of ion source 200°C; direct introduction of sample (vaporization temperature 45—65°C).

very pronounced in the low-energy spectra of arenes[5]—do *not* occur in the compounds under study (the molecular ions of the deuterated derivatives *(1c)* and *(1f)* lose exclusively $C_3H_3D_2^{\bullet}$) likewise indicates a kinetically fast process favored by the silyl and germyl groups. That the $[M-R]^+$ ions do indeed have an oxonium structure *(3)* is proved by the DADI spectra[6]. Those recorded for *(1a)*, *(1b)*, *(1c)*, *(4a)*, and *(4b)*—the last-named two yield an ion *(3)* by α cleavage which is used as reference structure—are identical with earlier published spectra of silylated fluorenonium ions *(3)*[1,7].



(5) (6)

A comparison of the electron impact induced transformation of the molecular ions *(1)* with the thermal reaction of the corresponding neutral molecule *(5)* is remarkable. At 160 to 195°C the silyl derivatives *(5)*, X = Si, undergo a formal dyotropic rearrangement[8] to give *(6)*, in which the O—C bonds are homolytically cleaved with anchimeric assistance[9]. In comparison, the *tert*-butyl derivative is completely thermally stable *(5)*, X = C, R = $CH_2C_6H_5$. For reasons not yet explained, this strict correspondence between thermal and electron impact induced behavior[1,4] does not apply to the analogous germyl compounds *(5)*, X = Ge. The latter decompose just like the silyl derivatives in the mass spectrometer but react slower by orders of magnitude on thermolysis[10].

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CAS Registry numbers:
(1a), 60512-32-5; *(1b)*, 60512-33-6; *(1c)*, 60512-34-7; *(1d)*, 60512-35-8; *(1e)*, 60512-36-9; *(1f)*, 60512-37-0; *(1g)*, 60512-38-1; *(4a)*, 60512-39-2; *(4b)*, 60512-40-5

[1] Mass Spectrometric Studies on Dyotropic Rearrangements, Part 2.—Part 1: *H. Schwarz, M. Kliment, M. T. Reetz*, and *G. Holzmann*, Org. Mass Spectrom. *11*, 989 (1976).

[2] Concerning the classification of this reaction, see *H. Schwarz* and *R. Wolfschütz*, Org. Mass Spectrom. *11*, 773 (1976).

[3] Whereas anchimeric effects, *i.e.* formation of three-membered cyclic transition states facilitated by neighboring group participation, have been frequently observed in the mass spectrometer (see, *e.g.*, *K. B. Torner, J. Turks*, and *R. H. Shapiro*, Org. Mass Spectrom. *6*, 235 (1972)), the corresponding neighboring group participation has not hitherto been observed with IVB metals; cf. *M. R. Litzow* and *T. R. Spalding*: Mass Spectrometry of Inorganic and Organometallic Compounds. Elsevier, Amsterdam 1973. Concerning the migration tendency of silyl functions see also: *H. Bosshardt* and *M. Hesse*, Angew. Chem. *86*, 256 (1974); Angew. Chem. Int. Ed. Engl. *13*, 252 (1974).

[4] With the silyl compounds neither the electron impact induced nor the thermally induced rearrangements are limited solely to fluorenyl derivatives. Radicals other than benzyl or allyl can also function as neutral component (cf. ref. [1] and ref. [9]).

[5] *J. T. Bursey, M. M. Bursey*, and *D. G. I. Kingston*, Chem. Rev. *73*, 191 (1973).

[6] Concerning the topic "Ion structures and properties of metastable ions" (*i.e.* also DADI spectra) see a) *R. G. Cooks, J. H. Beynon, R. M. Caprioli*, and *G. R. Lester*: Metastable Ions. Elsevier, Amsterdam 1973; b) *U. P. Schlunegger*, Angew. Chem. *87*, 731 (1975); Angew. Chem. Int. Ed. Engl. *14*, 679 (1975); c) *K. Levsen* and *H. Schwarz*, *ibid. 88*, 589 (1976) and *15*, 509 (1976).

[7] Since we have not yet been able to synthesize germyl derivatives having structure *(4)*, X = Ge, we cannot yet offer direct proof of the structures of the ions $[M-R]^+$ from *(1d)*, *(1e)*, and *(1f)* but only deduce analogous structures from the similar reactions of germyl and silyl ethers (see Table 1). The fact that the ionic yield curves for the $[M-R]^+$ ions from *(1a)* to *(1f)* display a relatively small slope (which is typical for rearrangements, cf. ref. [6a, c]) rules out a simple α cleavage of the O—C bond in which the liberated oxenium ion would be stabilized by hyperconjugation of the C-metal bond.

[8] For a definition, see: *M. T. Reetz*, Tetrahedron *29*, 2189 (1973).

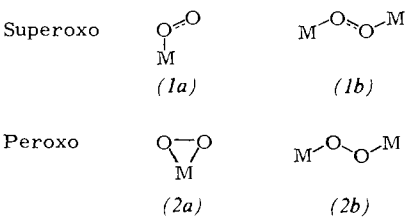
[9] *M. T. Reetz* and *M. Kliment*, Tetrahedron Lett. *1975*, 797.

[10] *M. T. Reetz*, unpublished results.

Reviews

Abstracts of selected progress reports and review articles

Dioxygen-metal complexes containing covalent bonds are reviewed in an article by *L. Vaska*. The most important types are superoxo [*(1a)*, *(1b)*] and peroxo compounds [*(2a)*, *(2b)*] (oversimplified diagrams). Nearly all transition metals form dioxygen complexes; the formal oxidation states of the



(1a) *(1b)* *(2a)* *(2b)*

metals in these species range from 2 through 6. Most of the complexes belong to the type *(2a)*. [Dioxygen-Metal Complexes: Toward a Unified View. Acc. Chem. Res. *9*, 175—183 (1976); 64 references]

[Rd 887 IE—L]

Genetics and biological evolution was the subject under discussion at the 4th FASEB (Federation of American Societies for Experimental Biology) conference. Main themes of the conference were selection and genetic drift in molecular evolution, function and evolutionary changes in proteins, origin of new proteins, evolution of multigene systems, evolution of membrane transport and selection of somatic cells. Numerous prominent authors contributed articles to each of the individual themes under discussion. [Genetics and Molecular Evolution. Fed. Proc. *35*, 2077—2204 (1976); 28 references]

[Rd 889 IE—R]

The self-association of tubulin has been examined from the physical-chemical point of view by *S. N. Timasheff*, *R. P. Frigon*, and *J. C. Lee*. The theory put forward by *Gilbert*[1] affords the basis for a quantitative treatment of such processes. Tubulin monomers undergo association equivalently; only the last (presumably the 26th) monomer associates with a higher constant since a cyclic structure can then be formed. Higher temperatures and the presence of Mg ions favor polymerization, whereas high pressures suppress formation of polymers. In glycerol-containing buffers, tubulin can even be reconstituted to complete microtubuli without requiring high-molecular nucleation centers. [A Solution Physical-Chemical Examination of the Self-Association of Tubulin. Fed. Proc. *35*, 1886—1891 (1976); 33 references]

[Rd 890 IE—R]

[1] *G. A. Gilbert*, Discuss. Faraday Soc. *20*, 67 (1955).

Protein-protein interactions in the regulation of lactose synthase is the theme of an article by *K. Brew* and *J. T. Powell*. Lactose synthase is known to be composed of a galactosyl transferase and α-lactalbumin. The normal substrate of galactosyl transferase is *N*-acetylglucosamine or glycoproteins which contain this sugar. α-Lactalbumin modifies the enzymatic activity of the transferase by reducing the Michaelis constant of the galactose receptor glucose by a power of three. Kinetic studies indicate an ordered sequential mechanism for substrate formation during the catalysis. α-Lactalbumin resembles in many respects lysozyme and thus probably also the glycoprotein substrates of the transferase. Interaction between α-lactalbumin and the transferase is influenced by substrates as well as by Mn^{2+} ions. [Substrate-Dependent Protein-Protein Interactions in the Regulation of Lactose Synthase. Fed. Proc. *35*, 1892—1898 (1976); 26 references]

[Rd 891 IE—R]

The interrelationship between arginine, glutamic acid and proline in metabolism and nutrition is the theme of an article authored by *R. E. Austic*. The chicken can produce only a part of its proline requirements; thus, proline becomes an essential amino acid. Although arginine, glutamic acid and ornithine can in principle be transformed into proline, these sources are insufficient to satisfy demand. It therefore remains to be investigated which enzymatic reactions are responsible for the bottleneck along the pathway from the mentioned amino acids to proline. [Nutritional and Metabolic Interrelationships of Arginine, Glutamic Acid and Proline in the Chicken. Fed. Proc. *35*, 1914—1916 (1976); 46 references]

[Rd 892 IE—R]

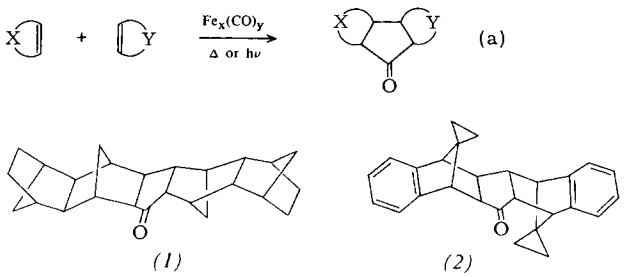
Subunit-subunit interactions of transcarboxylase are outlined in an article by *H. G. Wood*. This biotin-containing enzyme is present in propionic acid bacteria, where it catalyzes the transcarboxylation of methylmalonyl coenzyme A to pyruvate to propionyl coenzyme A and oxalacetate. In contrast to other biotin enzymes, free carbonic acid does not participate. The enzyme consists of several subunits. A central subunit comprises several (according to latest findings six) peripheral subunits linked together *via* a third and very flexible type. The subunits can be further dissociated and, in part, recombined. The individual units can be assigned to definite catalytic steps. [Subunit Interactions of Transcarboxylase. Fed. Proc. *35*, 1899—1907 (1976); 11 references]

[Rd 893 IE—R]

Nutritional and metabolic interrelationships among sulfur compounds in avian nutrition is reviewed by *D. H. Baker*. Bird foods generally contain cysteine as the limiting sulfur-containing amino acid. Economically, D,L-methionine or its hydroxy analog is usually employed in order to counter the deficiency in cysteine. Methionine can be converted into cysteine in the metabolism, but not the converse, most likely because the cystathionine synthetase reaction is irreversible. High doses of methionine are toxic, leading to emptying of the threonine pool. Inorganic sulfate can partly meet the sulfur requirement, but only the demand for cysteine and not for methionine decreases. Younger birds require choline. Methionine cannot fulfil this requirement. In older birds self-synthesis of choline suffices. [Nutritional and Metabolic Interrelationships among Sulfur Compounds in Avian Nutrition. Fed. Proc. *35*, 1917 to 1922 (1976); 65 references]

[Rd 894 IE—R]

The stereospecific formation of cyclic ketones from strained olefins and carbonyliron compounds is the theme of a report by *E. Weissberger* and *P. Laszlo*. Cyclopentanone derivatives such as *(1)* and *(2)* can be prepared in satisfactory yields (62 and 42 %, resp.) according to the general reaction (a). $Fe(CO)_5$, $Fe_2(CO)_9$ and $Fe_3(CO)_{12}$ are suitable iron(0) com-



ponents. [Stereospecific Cyclic Ketone Formation with Iron(0): Anatomy of an Interligand Reaction. Acc. Chem. Res. 9, 209—217 (1976); 60 references]

[Rd 895 IE—L]

σ-Bonded organic derivatives of f elements are reviewed in an article by *M. Tsutsui, N. Ely,* and *R. Dubois.* Most organoactinoid complexes with σ- and π-ligands belong to the $Cp_3U—R$ type compounds (cp = η^5-cyclopentadienyl, R = alkyl, aryl, alkynyl); an example is $Cp_3U—C{\equiv}C—C_6H_5$. The Cp_3U moiety can also occur as substituent in a ferrocenyl molecule. Organolanthanoid complexes include not only the $Cp_2Ln—R$ type but also the $CpLnR_2$ type, *e.g.* $CpHo(C{\equiv}C—C_6H_5)_2$. Whether f-orbitals participate in the covalent bonding has not as yet been unequivocally explained. The catalytic action of the complexes $Cp_3U—R$ (R = methyl, phenyl, benzyl) in the oligomerization of olefins has, on the other hand, already been proven. [σ-Bonded Organic Derivatives of f Elements. Acc. Chem. Res. 9, 217—222 (1976); 58 references]

[Rd 896 IE—L]

BOOK REVIEWS

Einführung in die Physikalische Chemie (Introduction to Physical Chemistry). By *H. Labhart.* Springer-Verlag, Berlin—Heidelberg—New York 1975. 1st edit. Part 1: Chemische Thermodynamik (Chemical Thermodynamics). xii, 167 pp., 38 figs., bound, DM 16.—; Part 2: Kinetik (Kinetics). x, 105 pp., 23 figs., bound, DM 13.60; Part 3: Molekülstatistik (Molecular Statistics), xi, 126 pp., 19 figs., bound, DM 14.—; Part 4: Molekülbau (Molecular Structure). x, 171 pp., 45 figs., bound, DM 16.—; Part 5: Molekülspektroskopie (Molecular Spectroscopy). x, 138 pp., 52 figs., bound, DM 16.—.

This "Introduction to Physical Chemistry", which had its origin in the author's lectures to chemistry students in their third to sixth semester at Zürich, is conceived in such a way that access to physical chemistry can be gained through the description of either macroscopic (Parts 1 and 2, also Part 3) or microscopic properties (Parts 4 and 5, also Part 3). The contents are selected in accordance with the above scheme. The author prefers the deductive approach of set purpose, and therefore stresses, *inter alia,* the limits of model representations and the nature of approximations. The selection of the material is consequently such as to be free from the need to base the teaching on as many facts as possible.

In its first four chapters, Part 1 provides the concepts and fundamental principles of thermodynamics. In Chapter 5 are described applications of thermodynamics to phase equilibria in one- and multicomponent systems as well as, relatively briefly, to reaction equilibria and electrochemical equilibria. The reviewer felt it was a disadvantage—and in fact this applies to all five Parts of the work—that relatively few arithmetical examples are provided and, furthermore, that there are no problems to check one's progress. In many places it would have been advantageous for the beginner to have more frequent indications of the practicability of an experiment and its evaluation. It should be noted that SI units are not used consistently.

Part 2 gives the foundations of reaction kinetics, and extends these by a chapter on transport phenomena, diffusion, heat conduction, and viscosity. Up to Chapter 5.4 the principles required for understanding kinetics are outlined. In Chapter 5.5 enzymatic reactions, photoreactions, and the pressure dependence of gas reactions are briefly reported. Chapter 6 shows the empirical dependences (temperature, solvent, structure) of rate constants in homogeneous reactions, and Chapter 8 provides an introduction to the theory of kinetic constants (rate constants, diffusion constants), this foreshadowing the concepts of molecular statistics worked out in Part 3.

In its first chapter Part 3 gives, in very concise form, the basics of molecular statistics and explains the connection with thermodynamic variables and calculation of partition functions. Applications of Maxwell-Boltzmann statistics are illustrated in the following Chapters 2 (gases), 3 (liquids), and 4 (solids). Solids and phase transition problems are mentioned only briefly in Part 3. On the other hand—presumably owing to the subdivision of the whole work—the predominantly experimental section concerned with electrolyte solutions is placed in Chapter 3.5.5, pages 88—100.

In Part 4 the principles are laid down for understanding the electronic structure of molecules, beginning with the time-independent Schrödinger equation. The postulates of quantum mechanics (Chapter 2.2) are outlined in a compact section (Chapter 2.1) with the aid of mathematics. After treatment of some one-particle problems (electron in a potential box of finite depth, oscillator, rotator, hydrogen atom) in Chapter 3, there follows in Chapter 4 a brief account of important approximation procedures for many-particle problems. The electronic structure of the atom is described in Chapter 5. Chapter 6 treats diatomic molecules with special reference to the H_2 molecule, and Chapter 7 polyatomic molecules and the HMO model. In Chapter 8, facts about empirical properties of molecules (shape, energy, charge distribution, reactivity) are presented and discussed on the basis of results of experimental methods of investigation (Part 5).

Part 5 describes spectroscopic methods for the investigation of molecules; an introductory chapter is followed in turn by sections on nuclear magnetic resonance, electron spin resonance, transitions between rotational states, transitions between vibrational states, transitions between electronic states, photoelectron spectroscopy, and X-ray fluorescence spectroscopy. Concentration on the generally most important methods currently available to chemists for the determination of molecular properties has here provided a compact and highly informative review.

Each of the five Parts has an appendix containing useful and important details and/or further derivations. The mathematical and physical background needed for the individual Parts varies, being highest in the first chapters of Part 4, but generally speaking all five Parts can be read easily and with interest.

Some problems of physical chemistry are only touched upon or not treated at all, *e.g.* surfaces, solid state, metals, magnetochemistry, and d-electron systems. However, this must not be considered a limitation, since the fundamental concept of the work necessitated concentrating on the main points.

Each of the five Parts can be used separately. Cross-references to concepts, formulas, *etc.* in other Parts are rare. This interesting work can be welcomed and recommended as a whole, and provides a worthwhile addition to currently available textbooks.

Wolfgang Haase [NB 340 IE]

Principles of Food Science. Part 1: Food Chemistry. Edited by *O. R. Fennema.* Marcel Dekker Inc., New York—Basle 1976. 1st edit., xi, 792 pp., bound, sfr. 170.—.

The interdisciplinary character of food science is illustrated by the make-up of this work, whose three parts are devoted to chemistry, microbiology, and technology of foodstuffs. The purpose of the present Part 1 is to review the structure and composition of foodstuffs, their properties, and chemical changes. The book is intended for advanced students and experts in neighboring fields who already have a sound basic knowledge of organic chemistry and biochemistry. The treatment begins with the main constituents of foods, such as water and ice, carbohydrates, lipids, and proteins, then substances occurring in lower concentrations such as enzymes, vitamins, and inorganic compounds, dyes, and flavoring substances, as well as other desirable or undesirable constituents or additives. Subsequent sections are directed at the structure of foodstuffs and describe the make-up and properties of muscle tissue and plant tissue, of dispersions, and of liquid foods such as milk and eggs. Each chapter is supplemented by numerous references to more recent work.

The 19 authors of the individual sections have all earnestly striven to seek out the important structural and chemical properties of foodstuffs and to clarify the relationships between the chemical reactions and the behavior of the food on storage or further processing. Other matters, such as questions of analysis, of biosynthetic connections between constituents, and special features of individual foodstuffs are thus often passed over. Even though the weight is in many places unevenly distributed, and many interesting details are omitted, the book gives a valuable and comprehensive reflection of the whole field and records the scientific principles of food chemistry on the basis of the most recent state of knowledge.

Hans-Peter Thier [NB 341 IE]

The Chemistry of Cyano Complexes of the Transition Metals. Organometallic Chemistry—A Series of Monographs. By *A. G. Sharpe.* Academic Press, London—New York—San Francisco, 1976. 1st edit., xi, 302 pp., bound, £ 10.40.

Written by an expert, this book provides as it were a supplement to the review of the chemistry of cyano complexes of the transition elements that appeared in "Advances in Inorganic Chemistry and Radiochemistry" *8*, 83 (1966). The selected arrangement begins with the cyano compounds of metals of the third subgroup, including the little that is known about complexes of the lanthanides and actinides, and finishes with complexes of metals of the second subgroup. This permits the reader to orient himself rapidly in the book, particularly because there is a vertical order within each chapter, with increasing oxidation number for each individual element. *Sharpe* does not take information uncritically from the literature, but comments from his own experience and directs attention to what is as yet unexplored. The result is thus quite different from a mere barren text. In the introduction—kept rather short—the general aspects are discussed, including methods of preparation and the structural chemistry of the cyano complexes. With normal vibrations it would have been better not to restrict the data to tetrahedral, square-planar and octahedral species, but to treat also the other types with coordination numbers of 2, 3, 5, and 7. A disadvantage of the book is the almost complete absence of illustrations and summarizing tables. Nevertheless, the book can be recommended to every complex chemist as a very reliable source of scientific information and stimulation.

Kurt Dehnicke [NB 343 IE]

Lehrprogramm Atombau und Periodensystem (Programmed Learning—Atomic Structure and the Periodic System) (Pocketbook 47). By *Christa Braig.* Verlag Chemie/Physik Verlag, Weinheim 1976. 1st edit., x, 146 pp., 40 figs., 2 foldout tables, paperback, DM 12.80.

Complaints are always voiced about the very variable chemical knowledge possessed by students beginning their study of natural science. The above pocketbook is designed to enable particularly those students who have been badly taught to make themselves familiar with atomic structure and the periodic system by a brief private course of study with the aid of two learning programs.

The learning program for atomic structure contains three chapters: the elementary particles within the atom, the atomic nucleus, and the electron shell. The program on the periodic system comprises the following sections: definition of concepts, the make-up of the periodic system, and the periodicity of some properties of main-group elements.

The subject matter is presented with beautiful clarity, and great care has been taken to avoid printing errors. The book seems very suitable for its readership.

The fundamental remarks about the model concept (p. 2) are particularly helpful to the beginner. From the reviewer's own experience it is by no means superfluous to give the mass of the proton (p. 5) with all the zeros. Under the keyword "Hund's rule" (p. 61) it might have been mentioned that this is only *one* of Hund's rules.

The further titles planned with a similar purpose will be welcome.

Hartmut Plautz [NB 346 IE]

Industrielle Organische Chemie (Industrial Organic Chemistry). By *K. Weissermel* and *H.-J. Arpe.* Verlag Chemie GmbH, Weinheim/B. 1976. 1st edit., xii, 378 pp., 32 figs., 20 foldout tables, linen bound, DM 68.—.

The authors of this modern book know current organic industry and its interrelationships both as a whole and in detail from their own experience, and their book provides the reader with highly topical information on the essential starting materials and intermediates. The problems and prospects of energy and raw material resources are described (15 pages) with particular reference to the wake of the oil crisis, followed by detailed treatment of the preparation, use, and importance of the basic products of industrial syntheses (35 pages), then successively olefins (20), acetylenes (10), 1,3-dienes (18), syntheses from carbon monoxide (17), oxidation products of ethylene (41), alcohols (17), vinyl-halogen and vinyl-oxygen compounds (18), components for polyamides (24), reaction products from propene (33), production and conversions of aromatic compounds (20), transformation products of benzene (38), and the oxidation products of xylene and naphthalene (17). The volume ends with an Appendix (30 pages) giving schemes of processes and products, definitions of specific reaction parameters, tradenames, and sources, and finally an index (16 pages).

The whole work is not a textbook of organic-chemical technology but rather an exact informative review of a large part of present-day organic chemical industry with brief flashbacks into history and prospects for the future.

The book is addressed to a wide circle of readers. The advanced student is shown industrial interrelations and the young chemist just going into industry or taking his first steps toward it is particularly borne in mind: the over-all picture of industrial organic chemistry, which he had hitherto had to piece together from a multiplicity of detail over a long period, can now be grasped within a few weekends. The book should really be presented to every chemist on being offered his first appointment.

On another level, the work is a valuable source of information for the experimental industrial chemist on processes, syntheses, and important production figures.

For the university lecturer it offers important industrial interrelationships, new directions, and research problems. Last but not least, because of its clear and uncomplicated language, the book can lead the chemist's colleagues in industry, be they engineers or salesmen, toward a better understanding of the often complex relationships.

From the didactic point of view, the division of the text into a main column, an extract containing important facts in a side margin, and at the end of the book schemes of products and processes covering all parts of the book is very helpful. The reading is uninterrupted by literature references; these do not appear in the text at all. In their place there is, at the end of the book, a collection of general and specialized literature (up to 1975) arranged by the text sections.

A work of this kind, containing snapshots of individual pieces of information about industrial organic chemistry, cannot remain up-to-date for very long. Production figures change quickly, manufactures are stopped or expanded, processes are improved or abandoned. The authors will thus endeavor to keep the information in line with current practice.

The production of the book is excellent. The reviewer did not find a single misprint in the text. However, not all the references were correctly given or were immediately traceable.

On page 63, line 5, it could also have been mentioned that *tert*-butyl methyl ether is a fuel additive harmless to the environment. In the treatment of hydroformylation on page 101, Section 6.1, it would have been desirable to mention that *Roelen* found not only propionaldehyde but also diethyl ketone to be formed on treatment of ethylene with CO/H_2. On page 93 there should have been a mention that BASF had previously studied the acetone-acetylene process for the preparation of isoprene and had produced this important monomer also by this process (Merling synthesis).

This successful and useful book should be widely distributed in the specialist circles and in related disciplines. Strongly recommended.

Willi Ziegenbein [NB 347 IE]

Physiologische Chemie. Eine Einführung in die medizinische Biochemie für Studierende der Medizin und Ärzte. (Physiological Chemistry. An introduction to medicinal biochemistry for medical students and doctors.) By *H. A. Harper, G. Löffler, R. E. Petrides*, and *L. Weiss*. Springer-Verlag, Berlin—Heidelberg—New York 1975. xii, 940 pp., 644 figs., 189 tables, bound, DM 88.—.

Among the recent textbooks on biochemistry and physiological chemistry the excellently illustrated, stimulatingly written, and didactically exceptional books by *Lehninger* and *Stryer* have set new standards. The present "Physiological Chemistry" from a team of German translators and collaborators, however, takes as standard the contents list of the "Gegenstandskatalogs für die ärztliche Vorprüfung" (Subject Catalog for Medical Examinations) and as its basis a valued but now conceptually outdated American work.

The textbook is in the main suited to the intended type of reader. Alongside the classical contents (cell components and cell metabolism), more space than usual is devoted to consideration of the chapter that is elsewhere neglected in "Biochemistry" (water and electrolyte balance, metabolism of various organs and compartments, contractile systems, hormones, immune systems, and finally nutrition). This often leads to repetitions which are not always in agreement as to facts (ascorbic acid).

The arrangement of the extensive material makes the book a kind of reference work for the application of biochemical knowledge in medical practice. This is also helped by the good style and of technique printing used. However, more than 20 striking errors in structural formulas should be noted, particularly those of nucleotides and heterocycles. Stereochemical errors are frequent. Weaknesses appear in the treatment of thermodynamic principles and in the structure of biopolymers. Unfortunately there are no excercises as a necessary element of checking one's progress.

This textbook cannot be recommended for students of biochemistry as the principal or subsidiary subject. It does not provide an impression of the broad intellectual and experimental achievements that have raised biochemistry to its present imposing level, nor does it familiarize the reader with modern trends of development; for example, plasmids (episomal DNA) are mentioned only once and are not included in the subject index. The scientist is given only an indirect glance at pathobiochemical deviations and some clinical diagnostic applications.

The "Gegenstandskatalog" has led to other, unfortunately also factually incorrect, recent textbooks. Whether "Harper, Löffler, Petrides, Weiss" will be adopted depends finally on the price, which far is exceeds that what students can afford to pay.

Dieter Palm [NB 334 IE]

Fine Particles. Aerosol Generation, Measurement, Sampling and Analysis. Edited by *B. Y. H. Liu*. Academic Press, London—New York—San Francisco 1976. 1st edit., xii, 837 pp., numerous figs., bound, $ 34.50.

This book is a collection of 34 lectures delivered at the Symposium on Fine Particles held in Minneapolis in 1975. It begins with reviews of the research activity in several geographic areas. Methods of producing aerosols are then described. Jet atomizers, ultrasonic atomizers, processes involving evaporation, powder sprays, periodic dispersion of a liquid stream, and other possibilities are discussed. The chapter on aerosol sampling contains contributions on size selective sampling on impactors and centrifuges, which can be considered not only as sampling apparatus but also as high-resolution size-analyzers. Chapter 4, on measurement and analysis of aerosols, contains discussions of optical particle-size analysis with and without the use of lasers, flame-ionization detectors, electrical methods of measurement, condensation nuclei counters, piezoelectric mass detectors, as well as mass detectors that make use of β-ray attenuation.

Some of the contributions are very detailed: for example, *O. G. Raabe*'s article on aerosol production takes up 54 pages with 212 references. This comprehensiveness almost completely closes the gaps between the individual contributions that naturally occur in a collection of lectures. The volume thus qualifies as one of the most complete books on modern experimental techniques for use in the aerosol field, and it can be assumed that it will soon be seen on the desk of every scientist concerned with aerosols.

Dieter Hochrainer [NB 345 IE]

Farbenlehre und Farbmessung. By *W. Schultze*. Springer-Verlag, Berlin—Heidelberg—New York 1975. 3rd revised edit., vii, 97 pp., 57 figs., bound, DM 32.—.

This book is currently the only Introduction in the German language to color measurement and its applications in daily industrial practice. Mathematical expositions are largely avoided, and with a few exceptions this certainly makes it easier to understand "color metrics".

Two-thirds of the contents are devoted to the principles of color measurement (*inter alia* the CIE system color coordinates X, Y, Z, apparatus for color measurement, evaluation of color differences) together with scattered references to physiology (*e.g.* color blindness), while the remainder deals with questions of immediate practical value (tolerances, principles of color match calculations, color depth and color saturation, color reproduction). In 86 text pages many aspects can be covered only superficially, which also means that some terms introduced in the first part of the book cannot be explained until later. The 135 literature references will certainly help those who want more detailed information.

This small book can be recommended as a useful and easily readable review to practical workers and to all who occasionally come into contact with color measurements.

Fritz Heinrich [NB 335 IE]

Hochdruck-Flüssigkeits-Chromatographie (High-Pressure Liquid Chromatography). By *H. Engelhardt*. Springer-Verlag, Berlin—Heidelberg—New York 1975. 1st edit., x, 213 pp., 52 figs., 17 tables, bound, DM 56.—.

As stated by the author in the Foreword, the object of this 200-page book is to provide the newcomer to high-pressure liquid chromatography with a review of the apparatus, separation processes, and applicability of the method. Little stress is laid on the theory of chromatographic separation, but rather on a detailed discussion of the components of a high-pressure liquid chromatograph. Pumping systems, detectors, carrier materials, and stationary phases are described in detail. In addition, the author gives a clear description of the four types of liquid chromatography, augmented by representative examples of applications, with the greatest emphasis on the parameters that influence a separation.

It must, however, be said that the main purpose of the work, giving the experimentalist decisive help in obtaining a high-pressure liquid chromatograph, is unfulfilled by the present book. Much of the information is only of academic interest, since on the one hand apparatus is described (*e.g.* detectors) that is not supplied commercially, and on the other hand the user will seldom be in the author's position to construct or rebuild apparatus as would follow from a study of the book. Most users will find it impossible for practical reasons to obtain components such as pumps and detectors from the various distributors. A complete working system from one manufacturer, selected for a specific planned application, is usually the better answer, even if the high hopes attached to it often fall short in reality.

Karl Zech [NB 342 IE]

BAG-Farben-Lexikon (BAG Color Lexicon). International Lexicon of Procedures and Methods for the Preparation, Use, and Testing of Varnishes, Paints, and Similar Protective and Decorative Materials for All Industrial and Commercial Uses. By *H. Hadert*. BAG Brunner Verlag AG, Zürich/Verlag Chemie, GmbH, Weinheim 1976. 1st edit., 356 pp., plastic, DM 95.—.

This is the first book of its kind in the German language. It is aimed not only at the specialist but also at the users of varnishes, varnish ingredients, pigments, dyes, solvents, *etc.* In this Lexicon is collected a wealth of keywords from the varnish, paint, leather, and printing ink industries. A large part of the keywords consists of the tradenames of products and apparatus; the remainder are chemical, physical, and industrial terms. At the end of the explanatory text for very many of the industrial products there is a reference to the "Index of Manufacturers and Suppliers" in which the supplier company will be found with its full postal address.

The Index of Manufacturers and Suppliers is at the end of the book; this part of the Lexicon is printed on yellow paper to facilitate its location. If the reader requires additional information about a commercial product he can apply directly to the suppliers without losing time in searching for the address.

Hartmut Grahmann [NB 348 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Separation and Purification Methods, Vol. 4. Edited by *F. S. Perry, C. J. van Oss*, and *E. Grushka*. Marcel Dekker, New York 1976. xii, 413 pp., bound, $ 32.50.

Solute-solvent Interactions, Vol. 2. Edited by *J. F. Coetzee* and *C. D. Ritchie*. Marcel Dekker, New York 1976. xi, 459 pp., bound, SFr. 125.00.

Anionic Surfactants, Part I. Edited by *W. M. Linfield*. "Surfactant Science Series", Vol. 7. Edited by *M. J. Schick* and *F. M. Fowkes*. Marcel Dekker, New York 1976. xi, 314 pp., bound, SFr. 115.00.

Beiträge zur Didaktik der Chemie. By *R. Krämer*. Verlag Moritz Diesterweg, Frankfurt 1976. 224 pp., paper, DM 28.00.

Methodicum Chimicum. A Critical Survey of Proven Methods and Their Application in Chemistry, Natural Science, and Medicine. Edited by *F. Korte*. Vol. 8: Preparation of Transition Metal Derivatives. Edited by *K. Niedenzu* and *H. Zimmer*. Academic Press, New York/Georg Thieme, Stuttgart 1976. x, 579 pp., bound, $ 110.00.

Molecular Spectroscopy, Vol. 4. Senior Reporters: *R. F. Barrow, D. A. Long*, and *J. Sheridan*. The Chemical Society, London 1976. viii, 279 pp., bound, £ 17.25.—A volume in the series "Specialist Periodical Reports".

The Infrared Spectra of Minerals. Edited by *V. C. Farmer*. Monograph 4 of the Mineralogical Society, London 1974. x, 539 pp., bound, £ 16.00.

Structure and Bonding, Vol. 27: Bonding Forces. Edited by *M. Simonetta, A. Gavezzotti, K. D. Warren*, and *O. Ermer*. Springer-Verlag, Berlin 1976. iv, 217 pp., bound, DM 64.00.

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Gaseous Chloride Complexes with Halogen Bridges—Homo-Complexes and Hetero-Complexes

By Harald Schäfer[*]

The chemistry of the gaseous halide complexes which have been observed in large numbers in recent years is discussed for the example of chlorides. *Homo-complexes*—dimeric or polymeric chloride molecules containing chlorine-bridge linkages [*e.g.* $(NaCl)_n$, $n=2$—4; $(CuCl)_n$, $n=2$—5; $(BeCl_2)_n$, $n=2$—4; Pd_6Cl_{12}]—occur through broad areas of the Periodic Table. Comparison of the dissociation enthalpy of such molecules with the vaporization enthalpy of the liquid chlorides is particularly informative. *Hetero-complexes* are formed from different chloride molecules by linkage through Cl bridges. Not only 1:1 complexes (*e.g.* $NaAlCl_4$, $TlPbCl_3$, $KThCl_5$, $CdPbCl_4$, $AlUCl_8$) but also larger molecules (*e.g.* $CoAl_2Cl_8$, $CrAl_3Cl_{12}$, Cu_2UCl_6, In_2UCl_{10}) are known. Types of formulas, structures, and above all the formation enthalpies of such complexes are discussed critically. Hetero-complexes are useful in chemical transport reactions, as aids in syntheses, and in gas-chromatographic separations (lanthanoids, actinoids). They also play a part in many industrial processes (chlorination of ores) and in recently developed types of high-pressure discharge tubes.

1. Introduction

In 1857, during the classical period of molecular-weight determinations by *Dumas*' method, *Sainte-Claire-Deville* and *Troost*[1–3] discovered the dimeric nature of the gaseous trichlorides of aluminum and iron. This was long regarded as a special case.

Although *Kossel*'s theory suggested that gaseous dimers of the type

Na^+Cl^-
Cl^-Na^+

would be formed, such molecules were only observed in 1948 by *Ionov*[4] with the aid of mass spectroscopy. This observation, however, had few repercussions, probably because of the language barrier. The existence of dimeric alkali-metal halides attracted attention a few years later on publication of molecular-beam experiments by *Kusch et al.*[5], which were supplemented by *O'Konski* and *Higuchi*'s electrostatic calculations[6]. Mass-spectroscopic observations then followed in many laboratories, and today dimeric chloride molecules are known for almost 50 elements[7].

The existence of still larger aggregates was first demonstrated in 1950 by *Brewer* and *Lofgren*'s discovery of the very stable Cu_3Cl_3 molecule in the gas phase[8].

We designate as *homo-complexes* all aggregates composed of identical monomers.

The combination of dissimilar monomers into hetero-complexes was first observed for gaseous $NaAlCl_4$ and $KAlCl_4$ (*Fischer* 1949[9]; *Grothe* 1950[10]); gaseous hetero-complexes were subsequently found to be common. Reviews of gaseous complexes of type AMX_n, where A = an alkali metal and X = F or Cl, are already available[11–14].

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Important new impetus was provided in 1970 by *Dewing*'s investigations[15] into the volatilization of dichlorides ($MgCl_2$, $CaCl_2$, $CoCl_2$, $NiCl_2$, *etc.*) in a current of the gaseous trichloride of aluminum or iron. This field is now in a phase of lively development, the main interest being centered on the discovery of the formulas of new gaseous complexes and their thermodynamic properties. Possible applications are also beginning to appear.

The stability of the complexes can be determined by current methods of measuring equilibria, such as: a) measurement of the total pressure above melts of the components and chemical analysis of the distillate; b) optical measurement of equilibria by means of ligand field spectra; c) mass-spectrometric analysis of the equilibrated gases; d) entrainment measurements. Chemical transport experiments can also yield important information.

2. Dimeric Chloride Molecules

2.1. Occurrence and Stability

In analogy to the known structure of the Al_2Cl_6 molecule it is assumed that the metal atoms in other dimeric halides are also linked by double halogen bridges, a structure that, with its high symmetry, is reasonable in view of the mainly ionic nature of the bonds.

Table 1 shows the dimeric dichlorides so far known and their dissociation enthalpies.

b) Gaseous dimers of lower stability are to be expected for the *pentachlorides* of *Nb, Ta, Mo, W, Tc, and Re*; $NbCl_5$, $TaCl_5$, $MoCl_5$, and $ReCl_5$ form molecular lattices composed of dimers, and $NbCl_5$ is known to dissolve in dimeric form in CCl_4[17]. Of the *lower chlorides* in this group only *one* gaseous dimer is known, namely W_2Cl_6[18]; this, however, is not considered here because it probably contains a W—W bond, just as metal-metal bonds are of decisive importance for many lower (solid) halides in this group. We consider here only those molecules that are held together by halide bridges only. The U_2Cl_{10} molecule not only occurs in the crystal lattice and in CCl_4 solution, but also has a considerable stability in the gas phase[19]; however, there are no data for the monomer and thus none for ΔH^0 (diss).

c) The solid chlorides of *Ru, Os, Rh, and Ir* decompose to the elements on heating. In the gas phase the monomeric chlorides occur only in low concentrations, even in the presence of chlorine. Appreciable concentrations of the dimers held together by Cl bridges are thus not to be expected.

d) Non-ionic forces play an important part for the chlorides of *Pd, Pt, Cu, and Ag*, which has the result that certain arrangements (bond angles, coordination figures) are favored that can be realized only on the formation of larger aggregates (Pd_6Cl_{12}, Pt_6Cl_{12}, Cu_3Cl_3, Ag_3Cl_3). In addition, there is thermal instability: $CuCl_2$ decomposes on heating into CuCl and Cl_2. The *planar* gas molecule Au_2Cl_6 is known, but the monomeric trichloride cannot be obtained owing to its thermal decomposition into $Au_2Cl_{2,g}$, Au_s, and Cl_2, so that the dissociation enthalpy cannot be measured by the usual methods. The properties of $Au_2Cl_{2,g}$ are still not known.

Table 1. Dissociation $(MCl_x)_{2,g} \rightleftharpoons 2\,MCl_{x,g}$
ΔH^0(diss, 298) in kcal/mol of dimer; values after [7] (for VCl_2 after [16]).

LiCl 49.5	$BeCl_2$ 24.0											BCl_3 (6)	C	N	O	F	Ne
NaCl 48.6	$MgCl_2$ 40.5											$AlCl_3$ 30.2	Si	P	S	Cl	Ar
			$TiCl_3$ 40.6				$FeCl_3$ 35.4										
KCl 45.0	$CaCl_2$ 50.3	$ScCl_3$ 47.6	$TiCl_4$ (9)	VCl_2 34	$CrCl_2$ 49.3	$MnCl_2$ 38.9	$FeCl_2$ 37.0	$CoCl_2$ 36.5	$NiCl_2$ 34.6	Cu	$ZnCl_2$ 26.5	$GaCl_3$ 21.6	$GeCl_4$ (8) $SnCl_4$ (9)	$AsCl_3$ (9)	Se	Br	Kr
RbCl 42.9	$SrCl_2$ 51.2	YCl_3 49.6	$ZrCl_4$ 15.3	$NbCl_5$ (12)	$MoCl_5$ (12)	Tc	Ru	Rh	Pd	Ag	$CdCl_2$ 27.3	$InCl_3$ 29.7	$SnCl_2$ 22.8	$SbCl_3$ 11.2	$TeCl_4$ (15)	I	Xe
CsCl 42.9	$BaCl_2$ 47.1	$LaCl_3$ 50.8	$HfCl_4$ 15.4	$TaCl_5$ (12)	WCl_5 (13)	Re	Os	Ir	Pt	Au	$HgCl_2$ 13.0	TlCl 29.1	$PbCl_2$ 30.5	$BiCl_3$ 15.4	Po	At	Rn
Fr	Ra	Ac															
		Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	$LuCl_3$ 49.6		
		$ThCl_4$ 31.0	Pa	UCl_4 26.1 UCl_5	Np	Pu	Am										

A distinct pattern can be recognized:

a) The dissociation enthalpies of the dimers decrease monotonically along the series LiCl, $BeCl_2$, BCl_3 and NaCl, $MgCl_2$, $AlCl_3$. In the higher periods, where the series can be followed to the tetra- and pentachlorides, the appearance of a maximum and a strong decrease on the transition MCl_3/MCl_4 are readily identifiable. It follows that filling of the coordination sphere plays an important part: the coordination number 4 with tetrahedral coordination of the central atom is energetically favored, its attainment is favorable, and exceeding it is unfavorable (cf. also $TiCl_3/TiCl_4$ and $FeCl_2/FeCl_3$).

e) The tendency to form dimers is naturally less well expressed among the nonmetal chlorides. The nonmetal atoms are shielded either by the halide ligands or by lone-electron pairs, so that there is no opportunity to increase the coordination number.

f) It is striking that there is no special place among the dissociation enthalpies for the halides of aluminum or of iron(III). The singularity of these (and similar) trihalides lies in the relatively low stability of the condensed phase and

the associated low vaporization temperature, the gas phase consisting mainly of dimers even though ΔH^0(diss) is not unusually large.

g) The molecules Ga_2Cl_2, Ga_2Cl_4[20–23], In_2Cl_2, and In_2Cl_4[21–24] have not been taken into consideration. It is not certain whether M—M bonds appear in these cases. It may be that Ga_2Cl_4 and In_2Cl_4 should be placed among the hetero-complexes as $GaCl \cdot GaCl_3$ and $InCl \cdot InCl_3$.

2.2. Dissociation of the Dimer and Vaporization of the Liquid Phase

Dissociation of the dimer and the liquid → gaseous monomer transition

$$(MCl_x)_{2,g} \rightleftharpoons MCl_{x,g} + MCl_{x,g}; \quad \Delta H^0(\text{diss}) \qquad (1)$$
$$(MCl_x)_{n,l} \rightleftharpoons (MCl_x)_{n-1,l} + MCl_{x,g}; \quad \Delta H^0(\text{vap,mono}) \qquad (2)$$

are related to one another insofar as the aggregate is smallest when $n=2$ and largest when $n=\infty$ (liquid). It is thus meaningful to compare ΔH^0(diss) and ΔH^0(vap,mono) with one another. This is done for a uniform reference state, namely the (absolute) boiling point of the chloride or, more exactly, the temperature Tb at which the vapor pressure of the monomer above the melt amounts to 1 atm. Since we do not have good experimental values available for the vaporization enthalpies of all chlorides, it is useful to replace ΔH^0(vap, mono, Tb) by $Tb \cdot \Delta S^0$(vap,mono, Tb):

$$\frac{\Delta H^0(\text{diss}, Tb)}{\Delta H^0(\text{vap,mono}, Tb)} = \frac{\Delta H^0(\text{diss}, Tb)}{Tb \cdot \Delta S^0(\text{vap,mono}, Tb)} = f$$

If ΔH^0(diss, Tb) and ΔH^0(vap,mono, Tb) are of the same magnitude, as is usually the case, then $f \approx 1$ and we have:

$$Q = \Delta H^0(\text{diss}, Tb)/Tb = f \cdot \Delta S^0(\text{vap,mono}, Tb) \approx 22\ \text{cal/K} \cdot \text{mol}$$

provided that ΔS^0(vap,mono, Tb) has the normal Trouton constant.

As shown in Table 2, the Q values are generally of the expected magnitude. Exceptions are discussed below:

In most cases the available data do not lead us to expect accuracy exceeding ± 3 cal/K·mol. The Q values often also need correction because when the vapor pressure was determined it was not known that the gas phase contained not only the monomer but also larger aggregates; thus, the value given for Tb in the literature is too low and Q is too large. However, the effect is not very serious. In spite of such uncertainties useful estimates of the dissociation enthalpies of the dimers can be obtained in this way.

The few examples with relatively large Q are particularly interesting. Two limiting cases can be distinguished:

a) ΔH^0(vap,mono, Tb) is still approximately equal to ΔH^0(diss, Tb) but *both* values are unusually large. Thus, ΔS^0(vap, mono, Tb) is also particularly large. This clearly occurs for $BeCl_2$ [ΔS^0(vap,mono, Tb) = 31.4 cal/K] and for $CrCl_2$ [ΔS^0(vap,mono, Tb) = 30 cal/K] and could indicate a polymeric structure of the melt (chain polymers analogous to the solid state?)

b) ΔH^0(diss, Tb) is appreciably greater than ΔH^0(vap, mono, Tb); in other words, $f > 1$; however, ΔS^0(vap, mono, Tb) is normal at ≈ 22 cal/K. This is so for LiCl [ΔS^0(vap, mono, Tb)] = 22.8 cal/K] and NaCl [ΔS^0(vap,mono, Tb) = 22.0 cal/K] as well as for $AlCl_3$ [ΔS^0(vap,mono, Tb) = 23.9 cal/K]. Other trichlorides ($TiCl_3$, $FeCl_3$, $GaCl_3$, $InCl_3$) should probably be aligned along these.—For *aluminum chloride* the following *model considerations* can be set up: It is known that the melt consists of Al_2Cl_6 molecules. If we neglect intermolecular forces, then ΔH^0(vap,Al_2Cl_6) = 0 and ΔH^0(vap, $AlCl_3$) = $^1/_2 \Delta H^0$(diss). Then, further, ΔH^0(diss)/ΔH^0(vap, $AlCl_3$) = $f = 2$, and finally $Q = \Delta S^0$(vap,$AlCl_3$, Tb) $\times f \approx 22 \times 2 \approx 44$ cal/K or, with the true vaporization entropy, $23.9 \times 2 = 47.8$ cal/K. This is an upper limit; the experimental value (Table 2) is $Q = 40.4$ cal/K.

Thermodynamic interpretation: If ΔH^0(vap,mono) = ΔH^0(diss), this implies that the vaporization enthalpy of the dimer is the same as that of the monomer, $\Delta H^0(vap,mono) = \Delta H^0(vap,dimer)$. However, since in general ΔS^0(vap,mono) > ΔS^0(vap,dimer), it follows that in these cases P(monomer) > P(dimer).

Finally, it must be remembered that although $Q = \Delta H^0$(diss)/Tb has indeed the dimension of entropy, it is not the standard entropy of dissociation, since P(dimer, Tb) ≠ 1 atm. In all cases a large value of Q indicates a (relatively) large concentration of the dimer.

Table 2. $Q = \Delta H^0$(diss, Tb)/Tb in cal/K·mol of dimer.

LiCl 27.7	$BeCl_2$ 28.6											B	C	N	O	F	Ne
NaCl 25.7	$MgCl_2$ 22.0											$AlCl_3$ 40.4	Si	P	S	Cl	Ar
			$TiCl_3$ 33.9				$FeCl_3$ 35.8										
KCl 24.4	$CaCl_2$ 21.1	$ScCl_3$ 32.9	$TiCl_4$	VCl_2	$CrCl_2$ 29.8	$MnCl_2$ 24.3	$FeCl_2$ 25.9	$CoCl_2$ 25.9	$NiCl_2$ 26.3	Cu	$ZnCl_2$ 25.0	$GaCl_3$ 35.7	$GeCl_4$	$AsCl_3$	Se	Br	Kr
RbCl 24.1	$SrCl_2$ 20.8	YCl_3 24.8	$ZrCl_4$ 23.2	$NbCl_5$	$MoCl_5$	Tc	Ru	Rh	Pd	Ag	$CdCl_2$ 20.6	$InCl_3$ 33.9	$SnCl_2$ 21.9	$SbCl_3$ 21.1	$TeCl_4$	I	Xe
CsCl 25.0	$BaCl_2$ 20.7	$LaCl_3$ 21.0	$HfCl_4$ 24.1	$TaCl_5$	WCl_5	Re	Os	Ir	Pt	Au	$HgCl_2$ 21.5	TlCl 25.5	$PbCl_2$ 21.9	$BiCl_3$ 19.2	Po	At	Rn
Fr	Ra	Ac															
		Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	$LuCl_3$ 25.0		
		$ThCl_4$ 22.9	Pa	UCl_4 21.7	Np	Pu	Am										

2.3. Relation to the Formation of Dimers on Sublimation of the Elements

The approximate equality of ΔH^0(diss, *Tb*) and ΔH^0(vap, mono, *Tb*) valid for many chlorides implies that energetically the shorter bond lengths in the dimer compensate approximately for the greater number of neighbors in the liquid state.

Pauling[25] and later *Goldfinger et al.*[26] concerned themselves with the relation between the dissociation enthalpy $D^0(M_2)$ of the dimer of an element M and the sublimation enthalpy ΔH^0(subl) of the monomer, using values applying to 0 K. They found $\alpha = \Delta H^0(\text{subl})/D_0^0(M_2)$ to range from 0.5 to 12. The value of the quotient α depends on the electronic configuration of M. For the chlorides the quotient $f \approx 1$, analogous to $1/\alpha$, is much less variable than the above mentioned range, and this is understandable because in the chlorides the various atoms M are shielded by Cl ligands.

3. Larger Homo-Complexes $(MCl_x)_n$ with $n = 3$—6

3.1. Model Considerations

The situation in which ΔH^0(diss, *Tb*) $\approx$ ΔH^0(vap, mono, *Tb*) in the dissociation of $(MCl_x)_n$ to MCl_x where $n = 2$ or ∞ can be generalized for other values of n. That will be done here for one model case.

In the general equation

$$(MCl_x)_n \rightleftharpoons (n-1)MCl_x + MCl_x; \quad \Delta H_n^0 \tag{3}$$

$(n-1)$ is the number of dissociation steps for complete breakdown of $(MCl_x)_n$ into monomers, and ΔH_n^0 $(n-1)$ is the *dissociation enthalpy per step*; in the model we regard this amount as independent of n. Then for the splitting of MCl_x out of the liquid phase $MCl_{x,l} \hat{=} (MCl_x)_\infty$, we have $\Delta H_\infty^0/(\infty - 1) = \Delta H_\infty^0/\infty = \Delta H^0$(vap, mono).

A value of $\Delta H^0/(n-1)$ that is independent of n also implies independence of the vaporization enthalpy from the number n of vaporizing molecules. If $\Delta H_n^0/(n-1) =$ const it follows further that, *e.g.*

$$(MCl_x)_2 + (MCl_x)_4 \rightleftharpoons 2(MCl_x)_3; \quad \Delta H^0 = 0 \tag{4}$$

and

$$(MCl_x)_6 \rightleftharpoons 2(MCl_x)_3; \quad \Delta H_n^0/(n-1) \tag{5}$$

If the ΔS^0 per dissociation step were constant, then (at a given temperature) the dissociation constants per step would also be constant, $K_{1,2} = K_{2,3} = K_{3,4} \ldots$

$$\begin{array}{lll} (MCl_x)_2 \rightleftharpoons MCl_x + MCl_x; & K_{1,2}; & n=2 \\ (MCl_x)_3 \rightleftharpoons MCl_x + (MCl_x)_2; & K_{2,3}; & n=3 \\ (MCl_x)_4 \rightleftharpoons MCl_x + (MCl_x)_3; & K_{3,4}; & n=4 \end{array}$$

$$(MCl_x)_4 \rightleftharpoons 4MCl_x; \quad K_{1,4} = K_{1,2} \cdot K_{2,3} \cdot K_{3,4} \tag{6}$$

or, generalizing,

$$(MCl_x)_n \rightleftharpoons nMCl_x; \quad K_{1,n} = K_{1,2}^{(n-1)} \tag{7}$$

Within the range of validity of this model higher polymers would then be observed only when the concentration of dimers is also large. If the concentration of dimers is small, then as n increases the concentration of higher aggregates falls rapidly below the limit of experimental detection.

3.2. The Real Situation

The term $\Delta H_n^0/(n-1)$ is temperature-dependent. For homogeneous gaseous equilibria of the type $(MCl_x)_n \rightleftharpoons nMCl_x$, however, $\Delta C_p/(n-1)$ is almost independent of n (for $n = 2 \ldots 10$). This means that the ΔH^0 balance of the dissociation steps within a gaseous system can be compared at any desired temperature. This is not the case when $n = \infty$, that is for vaporization of the monomer from the liquid phase. Here ΔC_p and thus T play appreciable roles; ΔH^0(vap, *Tb*) < ΔH^0(vap, 298 K). Therefore, values of $\Delta H_n^0/(n-1)$ calculated for vaporization are placed below in braces { }.

The larger homo-complexes, in which the metal atoms are linked through halogen atoms, can be divided into three groups according to the nature of the bonding.

3.2.1. Polymers with Mainly Ionic Bonding

Typical examples are the trimeric and tetrameric alkali-metal chlorides. Here it is seen that trimerization and tetramerization can, according to the model, be considered energetically as an intermediate stage between dimerization and condensation to the liquid phase; the dissociation enthalpy per step is almost constant within one system, as shown by the following values (cf. Table 3) (kcal; 298 K):

$\Delta H_n^0/(n-1)$: $Li_2Cl_{2,g}$ (49.5); $Li_3Cl_{3,g}$ (49.9); {$LiCl_l$ (46.6)}
$Na_2Cl_{2,g}$ (48.6); $Na_3Cl_{3,g}$ (48.0); $Na_4Cl_{4,g}$ (47.1); {$NaCl_l$ (48.9)}

Qualitative observations are also available for Li_4Cl_4[27].

Subdivision into the individual dissociation steps leads to Table 3.

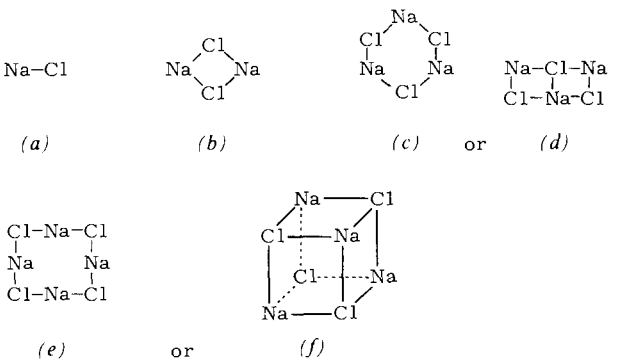
Table 3. Stepwise dissociation of $(LiCl)_n$ and $(NaCl)_n$.

Reaction	$\Delta H^0(298)$ [kcal]	$\Delta S^0(298)$ [cal/K]	$\Delta H^0(1000)$ [kcal]	$\Delta S^0(1000)$ [cal/K]	Ref.
$Li_2Cl_{2,g} \rightleftharpoons LiCl_g + LiCl_g$	49.5	32.7	48.3	30.7	[28]
$Li_3Cl_{3,g} \rightleftharpoons LiCl_g + Li_2Cl_{2,g}$	50.3	39.6	49.3	38.3	[28]
$LiCl_l \rightleftharpoons LiCl_g$	46.6	32.1	42.6	25.7	[28]
$Na_2Cl_{2,g} \rightleftharpoons NaCl_g + NaCl_g$	48.6	32.0	47.4	29.9	[28]
$Na_3Cl_{3,g} \rightleftharpoons NaCl_g + Na_2Cl_{2,g}$	47.3	38.8	46.4	37.8	[29] [a]
$Na_4Cl_{4,g} \rightleftharpoons NaCl_g + Na_3Cl_{3,g}$	(45.3)		(41.9)		[29] [a]
$NaCl_l \rightleftharpoons NaCl_g$	48.9	32.2	45.0	26.2	[28]

[a] Determined by data in [28] and estimated C_P values.

Constancy of the values of $\Delta H_n^0/(n-1)$ within the experimental error was observed previously for *oxides, e.g.* $(PbO)_n$ with $n=1-6$[30]; $(GeO)_n$ with $n=1-3$[31]; $(SnO)_n$ with $n=1-4$[32]; $(BeO)_n$ with $n=1-6$[28,33]; and $(WO_3)_n$ with $n=1-4$[28].

Here clearly there is a regularity that often occurs and that can be interpreted to mean that the energetic effect of increasing coordination with increasing n is largely compensated by the concomitant increase in bond lengths. This result is remarkable in view of the *structures* of the aggregates.



On the basis of IR spectra *Snelson*[34] concluded that Li_2F_2 had a planar ring structure and also considered a planar cyclic structure to be a possibility for Li_3F_3. According to calculations carried out by *Feather* and *Searcy*[29], for ionic bonds the structures *(e)* and *(f)* are energetically nearly equivalent for tetrameric NaCl; this is true, according to our own electrostatic calculations, also for structures *(c)* and *(d)* of the trimer. It should be noted that *(a)*, *(b)*, *(d)*, and *(f)* are sections from the structure of the NaCl crystal lattice.

Influence of reaction entropies: The model outlined in Section 3.1 was used for the case where, for the aggregation step, not only ΔH^0 but also ΔS^0 is constant. However, if we now examine the observed entropy values (Table 3) we see that there are considerable variations. The relatively large ΔS^0 values for the dissociation of the alkali-metal chloride trimers (and tetramers) have the result that their concentrations in saturated NaCl vapor decrease systematically starting from the dimers. This is clearly seen in the mass spectrum of saturated NaCl vapor (Table 4); cf. also the mass spectra of alkali-metal halides reported by *Berkowitz* and *Chupka*[27].

Table 4. Relative intensities of fragments in the mass spectrum of NaCl vapor saturated at 968 K, after *Feather* and *Searcy* [29]. The fragments arise mainly from the parent molecules specified.

Fragment	Relative fragment intensity	Parent molecule
Na^+	1.00	NaCl
$NaCl^+$	0.49	NaCl
Na_2Cl^+	0.88	Na_2Cl_2
$Na_3Cl_2^+$	0.0068	Na_3Cl_3
$Na_4Cl_3^+$	0.00010	Na_4Cl_4

The proportion of polymers in the vapor tends toward zero as the state of aggregation increases, this being in qualitative agreement with the original model.

From all the preceding considerations it follows that, with the means available today, aggregates with $n \geq 3$ will be detectable only if they can compete thermodynamically with condensation ($n=\infty$). *This is to be expected only for the chlorides with large values of Q.* It is thus not surprising that mass spectrometry has already led to the detection of Be_3Cl_6, Be_4Cl_8[35], Cr_3Cl_6, Cr_4Cl_8[37,38], Al_3Cl_9[39,40], Fe_3Cl_9[40], and Sc_3Cl_9[41]. For $(CrCl_2)_n$ we have quantitative data from *Rat'kovsky* and *Pribytkova*[37]; these correspond to the following $\Delta H_n^0/(n-1)$ values (980 K; values in kcal):

$Cr_2Cl_{4,g}$ (53); $Cr_3Cl_{6,g}$ (52); $Cr_4Cl_{8,g}$ (52)

The Mg_3Cl_6 molecule observed in small concentrations[42] does not fit into this scheme; here, however, the Q value is uncertain and the reported value may be too low.

3.2.2. Polymers in which Atomic Bonding Contributions Determine the Structures

$(CuCl)_n$ and $(AgCl)_n$ differ from polymeric alkali-metal halides in that the molecule with $n=3$ is considerably more stable than that with $n=2$. Only those members of the $(PdCl_2)_n$ and $(PtCl_2)_n$ series are formed for which $n=1$ and $n=6$. These facts must be interpreted as a preference for specific structures.

$(CuCl)_n$: Following the discovery of the Cu_3Cl_3 molecule by *Brewer* and *Lofgren*[8], the vapor of $(CuCl)_n$ was examined several times by mass spectroscopy[43-47]. That work substantiated the occurrence of Cu_2Cl_2, Cu_3Cl_3, Cu_4Cl_4, and Cu_5Cl_5; only at a higher temperature does monomeric CuCl become the main constituent of the gas phase. Assumption of Cu_6Cl_6 as an appreciable constituent[48] was contradicted by the mass spectra, which disclosed a clear fall in intensity along the series $Cu_3Cl_3^+$ (100), $Cu_4Cl_4^+$ (80), $Cu_5Cl_5^+$ (0.5). From measurements of the appearance energies[46] it follows that $Cu_3Cl_3^+$ cannot arise by fragmentation of Cu_6Cl_6.

Combination of the known formation enthalpy[28] or CuCl with the mass-spectroscopic data reported by *Guido et al.*[46] (and with estimated C_p values) enabled the following dissociation enthalpy per step to be evaluated; more recent values obtained by the same research group[45] are here given in parentheses; $\Delta H_n^0/(n-1)$ at 298 K in kcal for formation from the monomer are:

Cu_2Cl_2: not reported (43.5); Cu_3Cl_3: 63.5 (57); Cu_4Cl_4: 60 (54); Cu_5Cl_5: 57 (not reported); $CuCl_l$: 53.1[28].

The structure of the Cu_3Cl_3 molecule was determined by *Wong* and *Schomaker*[49] by electron diffraction to be a planar six-membered ring with $\sphericalangle CuClCu = 90°$. This is in agreement with the IR spectroscopic measurements (argon matrix) by *Cesaro et al.*[50]. The same authors assumed a strongly distorted cube as the structure of Cu_4Cl_4, but a planar ring structure seems more probable for Cu_4Cl_4 by analogy with Cu_3Cl_3, and also because the units $Cu_4O_4^{4-}$ and $Ag_4O_4^{4-}$, isoelectronic with Cu_4Cl_4 and Ag_4Cl_4, occur with square-planar ring structures ($\sphericalangle MOM = 90°$) in the crystal structure of KCuO, KAgO, and related compounds[51,52].

$(AgCl)_n$: Observations of the mass spectrum of silver chloride vapor are available from several groups[53-59]. In all cases the molecules AgCl and Ag_3Cl_3 were found as constituents of the vapor, but Ag_2Cl_2, Ag_4Cl_4, and Ag_5Cl_5 could also be observed by particularly sensitive measurements[56]. The disputed and rather improbable existence of the molecule Ag_3Cl_2 will not be considered in this review.

Below we use the ΔH^0 values obtained by *Wagner* and *Grimley*[56] from the temperature-dependence of the vapor pressure; the $\Delta H_n^0/(n-1)$ at 950 K in kcal for dissociation to the monomer are:

Ag_2Cl_2 (45.7); Ag_3Cl_3 (50.8); Ag_4Cl_4 (48.1); $AgCl_l$ (46.2)

The structures of the polymeric silver chloride molecules may well correspond to those of $(CuCl)_n$.

$(PdCl_2)_n$: On volatilization of $PdCl_2$ (350 °C) one observes only the ions $Pd_6Cl_{12}^+$ in the mass spectrometer at an electron energy of 15 eV; the vapor thus contains exclusively Pd_6Cl_{12} molecules[60]. Above 1000 °C monomeric $PdCl_2$ is the predominant molecule in the gas (equilibrium $Pd_s + Cl_2 \rightleftharpoons PdCl_{2,g}$[61]).

$(PtCl_2)_n$: If $PtCl_2$ is volatilized at 240 °C in the heating chamber of the mass spectrometer, the ions $(PtCl_2)_n^+$ can be observed, along with other fragments, with intensities that decrease as n goes from 6 to 1. From the determination of the appearance energies it follows that Pt_6Cl_{12} is the only parent molecule[44,62]. Monomeric $PtCl_{2,g}$ occurs in equilibrium with Pt and Cl_2 above 700 °C in concentrations that increase with rising temperature[63]. In the gas state Pd_6Cl_{12} and Pt_6Cl_{12} very probably have the same structure as that in the molecular lattice separable from the gas phase. This structure has been determined by X-ray structure analysis[60,64]. For $PdCl_2$ and $PtCl_2$ the preference for the hexamer rather than other stages of aggregation is clearly due to the fact that only this molecular structure permits all the Pd(Pt) atoms to assume square-planar coordination. The same coordination is found in the endless chains of solid α-$PdCl_2$. These facts are reflected in the ΔH^0 values as follows:

$$Pd_6Cl_{12,g} \rightleftharpoons 6\,PdCl_{2,g}, \quad \Delta H^0(298) = 306 \text{ kcal} \tag{8}$$

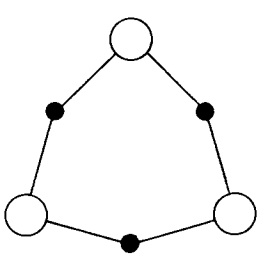
$$\alpha\text{-}PdCl_{2,s} \rightleftharpoons PdCl_{2,g}; \quad \Delta H^0(298) = 60 \text{ kcal} \tag{9}$$

$\Delta H_n^0/(n-1)$ at 298 K in kcal (values from [65]):
Pd_6Cl_{12} (61.2); $PdCl_{2,s}$ (60)

Similarly, for $PtCl_2$ (298 K; kcal[65]) we have:

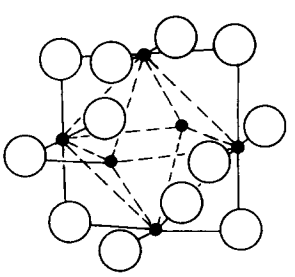
$\Delta H_n^0/(n-1)$: Pt_6Cl_{12} (55); $PtCl_{2,s}$ (54.9)

Because of structural analogies, the *solid* rather than the liquid dichloride is used for comparison in the above cases.



Cu_3Cl_3

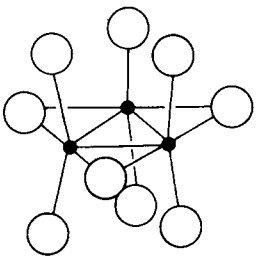
∢ CuClCu = 90°
∢ ClCuCl = 150°



Pt_6Cl_{12} and Pd_6Cl_{12}

3.2.3. Polymers with Cl Bridges and Metal-Metal Bonds

The most important representative of this class of compounds is Re_3Cl_9, whose structure in the molecular lattice has been determined by X-ray analysis[66,67].



Re_3Cl_9

The mass spectrum shows that the compounds vaporizes as Re_3Cl_9[68,69], and that the Re_3 unit is very stable. From the atomic separations it follows that the molecule is held together not only by Cl bridges but also by Re—Re bonds. A similar situation clearly occurs in the molecules W_3Cl_9[18] and Tc_3Cl_{12}[70] that have been observed by mass spectrometry. These clusters are mentioned here only to round off the picture.

4. 1:1 Hetero-Complexes

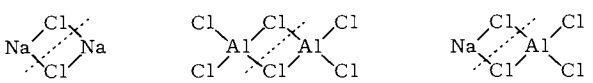
Just as the union of two identical monomers leads to the dimer (or 1:1 homo-complex), so 1:1 hetero-complexes arise from two different monomers, for example:

$$NaCl_g + AlCl_{3,g} \rightleftharpoons NaAlCl_{4,g} \tag{10}$$

A summary of the present state of knowledge is provided by Table 5.

It is advantageous to write the equation for complex formation in a form such that the coordination numbers do not change, *i.e.* starting with dimers, thus:

$$\tfrac{1}{2}\,Na_2Cl_2 + \tfrac{1}{2}\,Al_2Cl_6 \rightleftharpoons NaAlCl_4 \tag{11}$$



A general formulation is:

$$\tfrac{1}{2}\,A_2 + \tfrac{1}{2}\,B_2 \rightleftharpoons AB \tag{12}$$

For such a process the entropy balance $\Delta S^0 \approx$ zero if the slight influence of the symmetry number σ is neglected:

$$\Delta S_\sigma^0 = -R \ln \left[\frac{\sigma(AB)}{(\sigma(A_2)\cdot\sigma(B_2))^{1/2}} \right]$$

Furthermore, ΔC_p = zero is a good approximation. Finally, ΔH^0 will also depart little from zero[107] because the bonds in the reactants and products are similar in kind and number. Differences between A and B have only slight effect beyond the chlorine bridges:

$$\Delta H^0(AB) = \tfrac{1}{2}\,\Delta H^0(A_2) + \tfrac{1}{2}\,\Delta H^0(B_2) + Y \tag{13}$$

This approach is similar to *Pauling*'s classical derivation of electronegativity. The importance of Y is clearly as follows: dimerization enthalpies of about 50 chlorides are known; their combination leads to $n(n-1)/2 = 1225$ hetero-complexes

Table 5. 1:1 Hetero-complexes. Cf. [71]; the references cited there are not repeated here.

Valence of the cations	Complexes observed
1,1	$AA'Cl_2$ (A,A' = Li...Cs, cf. Table 7) $NaCuCl_2$ [72]; $TlCuCl_2$ [47] $AAgCl_2$ (A = Li...Cs) [73]
1,2	$NaBeCl_3$; $KBeCl_3$; $KMgCl_3$; $KCaCl_3$; $KSrCl_3$ $ACrCl_3$ (A = K, Rb, Cs) [74—76] $AMnCl_3$ (A = Li...Cs) [77—79] $AFeCl_3$ (A = Li...Cs) [78, 80, 81] $ACoCl_3$ (A = Li...Cs) [82, 83] $NaZnCl_3$; $KZnCl_3$ [84]; $TlZnCl_3$ [109] $ACdCl_3$ (A = Na...Cs, Tl) $ASnCl_3$ (A = Na...Cs) [85—87] $APbCl_3$ (A = Na...Cs, Tl)
1,3	$AAlCl_4$ (A = Li...Cs) [88]; $CuAlCl_4$ [47, 89, 165]; $AgCl/AlCl_3$ [89] $GaGaCl_4$ [20]; $BiAlCl_4$ [90] $InInCl_4$ [24]; $AInCl_4$ (A = K, Cs) [91, 92]; $TlInCl_4$ [47]; $CuInCl_4$ [47] $TlTlCl_4$ [24] $AFeCl_4$ (A = Na, K) $AScCl_4$ (A = Li...Cs) [41] $AYCl_4$ (A = Li, Na) [93] $ALnCl_4$ (A = Li...Cs, cf. Table 9) $NaBiCl_4$ [94]
1,4	$KThCl_5$ [95]; $AThCl_5$ (A = Tl, Cu, Ag) [47] $AUCl_5$ (A = Tl, Cu) [47]
1,5	$NaCl/NbCl_5$ [96]
2,2	$CdPbCl_4$
2,3	$BeAlCl_5$; $BeFeCl_5$; $BeInCl_5$ $ZnInCl_5$; $SnInCl_5$ $HgAlCl_5$ [97]; $SnBiCl_5$ [98]
2,4	$BeZrCl_6$; $BeUCl_6$; $PbThCl_6$ [99]
3,3	$AlGaCl_6$ [100]; $AlVCl_6$ [101]; $AlFeCl_6$ [40, 102, 166]; $AlCl_3 \cdot AuCl_3$ [89] $AlSbCl_6$; $AlBiCl_6$ [103] $GaInCl_6$ [104]; $AlInCl_6$ [167] $FeAuCl_6$ $EuLuCl_6$ [105]
3,5	$AlUCl_8$; $InUCl_8$ $AlCl_3/PCl_5$ [106]
4,4	$ThUCl_8$

of the 1:1 type; given useful rules for the value of Y, we have available the formation enthalpies of these complexes and can use them in thermodynamic calculations. We give below, therefore, a systematic tabulation of the Y values so far as present experimental findings permit.

1) For *compounds* $MM'Cl_x$ *not containing an alkali metal*, Y is zero within the limits of experimental error (Table 6).

Table 6. Y values (298 K) for alkali-free 1:1 hetero-complexes in kcal/mol complex; data without references are cited from [108].

$TlZnCl_3$ (−3.9) [109]; $TlCdCl_3$ (−1.7); $TlPbCl_3$ (−3.4); $TlInCl_4$ (+0.7); $TlThCl_5$ (−1.5); $TlUCl_5$ (−2.9); $CdPbCl_4$ (−1.9); $BeInCl_5$ (+1.1); $ZnInCl_5$ (+2.8); $SnInCl_5$ (+0.9); $PbThCl_6$ (−1.3); $AlGaCl_6$ (−0.7) [100]; $AlInCl_6$ (−1.8) [167]; $AlFeCl_6$ (0) [166]; $GaInCl_6$ (+0.7) [104]; $EuLuCl_6$ (+2.5) [105]; $AlUCl_8$ (+1.3) [19]; $ThUCl_8$ (−0.9)

2) In *combinations of two alkali-metal chlorides* $AA'Cl_2$, Y is small, but becomes noticeably more electronegative with increasing difference between the binary components (Table 7).

Table 7. Y value (*ca.* 1000 K) for mixed alkali-metal chloride 1:1 complexes in kcal/mol complex.

	LiCl	NaCl	KCl	RbCl	CsCl
LiCl	0				
NaCl		0			
KCl		−1.6 [110]	0		
RbCl		−5.8 [11]	0 [11] −1.1 [110]	0	
CsCl	−7.9 [11] −5.6 [111]	−5.2 [11]	−2.7 [11]	−1.0 [110]	0

The Y values in Table 7 are valid for approximately 1000 K with $\Delta S^0(1000) \equiv 0$. If the symmetry number is lowered by writing $\Delta S^0 = R \ln 2 = 1.38$ cal/K, then the Y values become 1.38 kcal more positive.

3) *Hetero-complexes* $AMCl_x$ *with* A = *an alkali metal* are distinctly more stable than the hetero-complexes discussed under headings 1 and 2. Admittedly, determination of reliable thermodynamic data meets here with special difficulties because of the coexistence of several gaseous complexes (cf. Section 6) and/or because of the occurrence of melts as bottom components. In some cases this leads to abnormal results for the reaction entropy, in other cases to a wide scatter of the derived thermodynamic values. The compilation in Table 8 is a critical selection from the extensive literature. Some cases have been newly evaluated. In all cases ΔH^0 was recalculated for 298 K by introducing estimated ΔC_p values. For $CsLuCl_4$, see below.

Table 8. Y values (298 K) for 1:1 hetero-complexes that contain one alkali-metal atom; in kcal/mol complex.

$KMgCl_3$	−17.3 (±5) [112]	$KScCl_4$	−12 (±2) [41]
$KCaCl_3$	−17.4 (±4) [112]	$KLaCl_4$	−17.5 (±3) [113]
$NaAlCl_4$	−13.0 (±3) [9, 108]	$CsLuCl_4$	−11 (±4)
$NaSnCl_3$	−16.3 (±3) [85]	$NaCuCl_2$	− 6.8 (±3) [72]
$KSnCl_3$	−16.1 (±3) [86]	$NaZnCl_3$	− 4.5 (±2) [114]
$RbSnCl_3$	−16.2 (±3) [87]	$LiFeCl_3$	− 1 (±2) [115]
$CsSnCl_3$	−16.2 (±3) [87]	$NaFeCl_4$	− 8.8 (±2) [116]

Table 8 gives the impression that the Y values for the main-group elements M are more uniform (−13 to −17 kcal) than for the transition elements M (−1 to −17 kcal). New measurements are urgently needed.

For the systems $ACl/SnCl_2$ (Table 8), $ACl/LnCl_3$ (Table 9), and $ACl/ScCl_3$[41] the value of Y is almost independent of the nature of the alkali-metal atom (A = Li...Cs).

Combinations of alkali-metal chlorides with lanthanoid chlorides were studied by *Novikov et al.* (Table 9): these authors determined values of ΔH^0 and ΔS^0 for the formation of $ALnCl_{4,g}$ from ACl_g and $LnCl_{3,g}$ by means of the temperature-dependence of the equilibrium position. To keep the influence of experimental errors small, Table 9 contains ΔG^0 values for the mean measurement temperature (1350 K) and not the ΔH^0 values. There is then no detectable variation of the stabilities of the complexes in the series of rare-earth metals (as for Li...Cs).

Clearly the ΔG^0 (1350) for all the unmeasured combinations $AlnCl_4$ can be estimated with good accuracy by means of Table 9. For conversion to other temperatures the introduction of $\Delta S^0(298) = -36$ cal/K and $\Delta C_p = 3$ cal/K is recommended.

Table 9. ΔG^0(1350 K) for $ACl_g + LnCl_{3,g} \rightleftharpoons ALnCl_{4,g}$; kcal/mol.

	Y	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
Li	−12.6 [93]								−18.0 [117]		−14.7 [118]					−13.3 [119]
Na	−16.3 [120]	−25.5 (?) [121]			−17.3 [122, 123]								−17.1 [122]			
K	−16.8 [113]	−18.8 [113]	−17.0 [124]	−15.3 [124]	−15.3 [124]								−15.8 [125]			
Cs					−17.0 [126]						−15.6 [127]		−16.4 [126]			−11.4 [119]

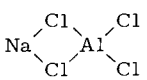
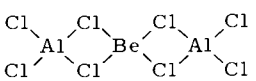
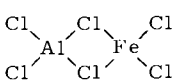
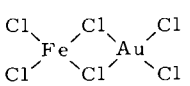
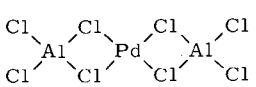
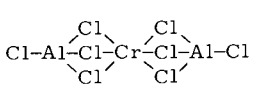
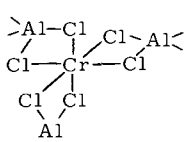
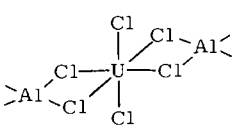
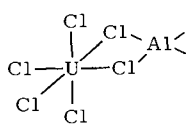
The Y value for the extreme case $CsLuCl_4$ (Table 8) was obtained in this way.

5. Larger Hetero-Complexes

5.1. Review, Formula Types, Structures

It is apparent from Table 10 that many large hetero-complexes are known.

The following structural types are characteristic and show clearly the importance of filling the coordination sphere:

Molecule			Coordination
$NaCl \cdot AlCl_3$		[A]	Na (2); Al (4, tetr.) C_{2v} symmetry
$BeCl_2 \cdot 2\,AlCl_3$		[B]	Al (4, tetr.); Be (4, tetr.)
$AlCl_3 \cdot FeCl_3$		[C]	Al (4, tetr.); Fe (4, tetr.)
$FeCl_3 \cdot AuCl_3$		[D]	Fe (4, tetr.); Au (4, plan.)
$PdCl_2 \cdot 2\,AlCl_3$		[E]	Al (4, tetr.); Pd (4, plan.) [130]
$CrCl_2 \cdot 2\,AlCl_3$		[F]	Al (4, tetr.); Cr^{II} (6, oct.) [128] analogous to $NiAl_2Cl_8$ [130]
$CrCl_3 \cdot 3\,AlCl_3$		[G]	Al (4, tetr.); Cr^{III} (6, oct.) [141]
$UCl_4 \cdot 2\,AlCl_3$		[H]	Al (4, tetr.); U^{IV} (6, oct.)
$UCl_5 \cdot AlCl_3$		[I]	Al (4, tetr.); U^{V} (6, oct.) [19]

In $NaAlCl_4$ [A] the position of the Na atom is uncertain (whether at a corner, edge, or face of the $AlCl_4$ tetrahedron), but it is probably above one edge (cf. also $NaAlF_4$[142] and $LiAlF_4$[143]).

The structure [B] given for $BeAl_2Cl_8$ is based on the existence of molecules $AlCl_3(BeCl_2)_nAlCl_3$ with $n=1$ to 3 and their probable relation to the tetrahedron chains $(BeCl_{4/2})_\infty$ in the structure of solid $BeCl_2$; cf. $BeCl_2/FeCl_3$ and $BeCl_2/InCl_3$ (Table 10). The structures [E] to [G] and [I] correspond to the observed ligand field spectra. The spectra measured for $CoCl_2 \cdot 2AlCl_3$ have not yet led to an unambiguous

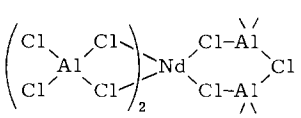
Table 10. Larger hetero-complexes. Cf. [71]; the references given there are not repeated here.

Valence of the cations	Complexes observed
1,1	$LiCs_2Cl_3$ Li_2CuCl_3, $LiCu_2Cl_3$; $NaCu_2Cl_3$ [72] $TlCu_2Cl_3$ [47]; A_2AgCl_3, AAg_2Cl_3 (A = Li...Cs) [73]
1,2	$Na_2Zn_2Cl_6$; $CsCd_2Cl_5$; K_2CdCl_4 (?) [84]
1,3	K_3InCl_6 (?) [91] Cu_2AlCl_5, Cu_3AlCl_6, $CuAl_2Cl_7$, $Cu_2Al_2Cl_8$ [47] AgCl/$AlCl_3$ [89, 96] Cu_2InCl_5, Cu_3InCl_6, $CuIn_2Cl_7$ [47] Tl_2InCl_5 [47]
1,4	Cu_2ThCl_6, $CuTh_2Cl_9$; Cu_2UCl_6 [47] Tl_2ThCl_6; Tl_2UCl_6; TlU_2Cl_9 [47]
2,3	Be_2AlCl_7, $BeAl_2Cl_8$, $Be_2Al_2Cl_{10}$, $Be_3Al_2Cl_{12}$ Be_2InCl_7, $BeIn_2Cl_8$, Be_3InCl_9 $BeFe_2Cl_8$, $Be_2Fe_2Cl_{10}$, $Be_3Fe_2Cl_{12}$ *MAl_2Cl_8* (M = Mg, Ca, Mn, Co, Ni, Pb); M = Cr [128, 129], M = Pd [130], M = Pt [131], M = Co [132—135], M = Cu [135, 136] *MFe_2Cl_8* (M = Mn, Co, Ni, Cd); (M = Mg, Ca, Sr, Ba) [135] *$MCl_2/AlCl_3$* (M = Fe, Cu, Ba) [96]; M = V [137] *$MCl_2/GaCl_3$* (M = Co, Ni) [96, 135] *$MCl_2/FeCl_3$* (M = Fe, Cu) [96]; M = Pd [89] *MAl_3Cl_{11}* (M = Mg, Ca, Mn, Co) $CoAl_4Cl_{14}$ [133]; VAl_3Cl_{11} [101]
2,4	Be_2UCl_8
3,3	Al_3CrCl_{12}; Al_3NdCl_{12}; Al_4NdCl_{15}; VAl_2Cl_9 [101]; $FeAl_2Cl_9$ [40] *$MCl_3/AlCl_3$* (M = Sc, Y, La, Mo) [96]; (M = Ru, Rh, Ir) [89]; M = Ln [138, 139]; M = U [140]; (M = Pu, Am, Cm) [139] $CrCl_3/GaCl_3$ [96] *$MCl_3/FeCl_3$* M = Y [96]; M = Ir [89] $GdCl_3/FeCl_3$ [135]
3,4	Al_2UCl_{10}; In_2UCl_{10} $ThCl_4 \cdot n\,AlCl_3$ (probably $n = 2$) [96]
3,5	$CrCl_3 \cdot m\,NbCl_5$ (probably $m = 3$) [96]

interpretation between tetrahedral and octahedral coordination of the Co[132, 133].

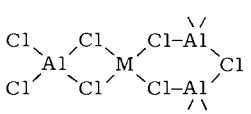
The formulas of the gaseous complexes [K] to [N] require the *structural unit* Al_2Cl_7 (cf. Section 6).

$NdCl_3 \cdot 4\,AlCl_3$ [144]



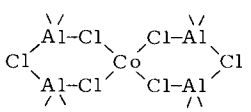
[K]

$MCl_2 \cdot 3\,AlCl_3$ [15]
M = Mg, Ca, Mn, Co



[L]

$CoCl_2 \cdot 4\,AlCl_3$ [133]

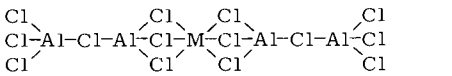


[M]

The structural group Al_2Cl_7, which is obviously very mobile at the Al—Cl—Al angle, is known to be bent in the crystal lattice of the compound $Te_4(Al_2Cl_7)_2$[145] and straight in melts[146] containing the equilibrium:

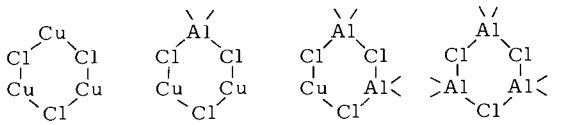
$$2\,AlCl_4^- + Al_2Cl_6 \rightleftharpoons 2\,Al_2Cl_7^- \qquad (14)$$

In the cases of $TiCl_2$, VCl_2, $CrCl_2$, $MnCl_2$, $FeCl_2$, $CoCl_2$, $NiCl_2$, and $CuCl_2$ in $AlCl_3$ melts the octahedral Cl-coordination of all the named M^{2+} follows from the ligand field spectra. The structure [N] is assumed for these complexes[147].

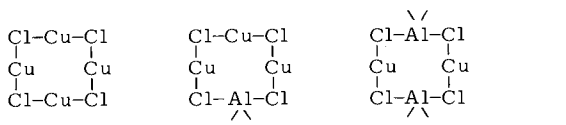


[N]

Ring structures, such as are known for Cu_3Cl_3[49] and assumed for Cu_4Cl_4, Ag_3Cl_3, and Al_3Cl_9, clearly also occur among the heterocomplexes. This is indicated by the series of compounds [O] and [P].



Cu_3Cl_3 Cu_2AlCl_5 $CuAl_2Cl_7$ Al_3Cl_9 [O]



Cu_4Cl_4 Cu_3AlCl_6 $Cu_2Al_2Cl_8$ [P]

The formulas of many complexes require coordinations that are unknown among *solid* chlorides, *e. g.* the coordination numbers 3 and 5 in the molecules $TlPbCl_3$ and $TlThCl_5$. Furthermore, for the $BeAlCl_5$ molecule it appears reasonable to discuss the arrangement of two face-bonded tetrahedra, although face-bonded tetrahedra are avoided in crystal structures. The infinitely extended anion packing in coordination lattices can place at the disposition of the cations positions that are energetically more favorable than is possible with small molecules. Care is therefore needed in drawing conclusions about the structure of molecules from the coordination polyhedra in crystals; this is also true when a compound has "accidentally" the same analytical composition in the solid state and in the gas phase.

5.2. Thermodynamics

Dewing[15] and *Papatheodorou*[131] have previously pointed out that the ion M^{2+} in the gaseous complex MAl_2Cl_8 is bonded similarly to that in the solid dichloride MCl_2. In both cases the M^{2+} is surrounded by Cl^- ions. Closer examination shows that there is a definite connection between the change in coordination number (ΔC.N.) on complex formation and the ΔH^0 balance: a loss of coordination energy shifts the ΔH^0 balance toward more positive values [cf. (15)—(19)].

$$\underset{\text{C.N. } 6}{NaCl_s} + \underset{6}{FeCl_{3,s}} \rightleftharpoons \underset{2\ 4}{NaFeCl_{4,g}};\ \Delta H^0(298) = +39\,\text{kcal};\ \Delta\text{C.N.} = -6 \qquad (15)$$

$$\underset{\text{C.N. } 6}{NaCl_s} + 0.5\,\underset{4}{Fe_2Cl_{6,g}} \rightleftharpoons \underset{2\ 4}{NaFeCl_{4,g}};\ \Delta H^0(298) = +22\,\text{kcal};\ \Delta\text{C.N.} = -4 \qquad (16)$$

$$\underset{\text{C.N. } 2}{0.5\,Na_2Cl_{2,g}} + \underset{6}{FeCl_{3,s}} \rightleftharpoons \underset{2\ 4}{NaFeCl_{4,g}};\ \Delta H^0(298) = +8.5\,\text{kcal};\ \Delta\text{C.N.} = -2 \qquad (17)$$

$$\underset{\text{C.N. } 2}{0.5\,Na_2Cl_{2,g}} + \underset{4(+x)}{FeCl_{3,l}} \rightleftharpoons \underset{2\ 4}{NaFeCl_{4,g}};\ \Delta H^0(298) = 0\,\text{kcal};\ \Delta\text{C.N.} = (-x) \qquad (18)$$

$$\underset{\text{C.N. } 2}{0.5\,Na_2Cl_{2,g}} + \underset{4}{0.5\,Fe_2Cl_{6,g}} \rightleftharpoons \underset{2\ 4}{NaFeCl_{4,g}};\ \Delta H^0(298) = -8.8\,\text{kcal};\ \Delta\text{C.N.} = 0$$

Similar results are found for other systems. (19)

If in reactions of the type solid + gas ⇌ gaseous complex the solid reactant is so chosen that the change in coordination number ΔC.N. on formation of the complex remains as low as possible, then the reaction enthalpy corresponds approximately to the heat of fusion of the solid component (cf. Table 11): the loss of coordination energy occurring on the solid → gaseous complex transition is of similar magnitude to that in the solid → liquid transition. This can be useful in estimations.

The following observations a) to d) are in accord with these considerations:

a) The complex $CoAl_2Cl_8$ is distinctly more stable than the corresponding nickel complex. This is also reflected in the greater rate of transport of $CoCl_2$ in chemical transport experiments. The heats of fusion of $CoCl_2$ and $NiCl_2$ differ in the same direction (Table 11).

b) Chemical transport experiments with $MoCl_2/Al_2Cl_6$ and WCl_2/Al_2Cl_6 at 500/400 °C proved negative[151]. These dichlorides have the structural formula $[M_6Cl_8]Cl_2Cl_{4/2}$. The solid state is stabilized not only by chlorine bridges but also by metal-metal bonds in the octahedral M_6 groups. Gas complexes which do not contain metal-metal bonds cannot compete energetically. The absence of $AlCl_3$ complexes with $MoCl_2$ or WCl_2 and the existence of such complexes with $CrCl_2$ can be ascribed to the structure of the solid dichlorides. The fact that the dichlorides $PdCl_2$ and $PtCl_2$, which contain no metal-metal bonds, can form gaseous complexes with $AlCl_3$ (*i.e.* MAl_2Cl_8) in spite of their cluster structure (M_6Cl_{12}) fits into this picture.

c) According to the views expressed above, the ΔH^0 for complex formation as in Table 11 should be independent of the nature of the readily volatilized reactant formulated as dimer M_2Cl_6[Al_2Cl_6, Fe_2Cl_6, Ga_2Cl_6...]. In fact the reactions affording the Fe^{III} complexes are only 2 kcal/mol more strongly endothermic than those affording the Al complexes.

d) Reactions 14 and 17 in Table 11 are also noteworthy. In both cases $UCl_{4,s}$ is converted into the complex with C.N. = 6, while the Al or Tl retains its coordination number unchanged. The ΔH^0 values are thus almost equal.

Table 11. Thermodynamic data for the formation of gaseous complexes. Literature data partly re-evaluated (cf. [108]) [a]. ΔH^0(melt) refers to solid reactants at their melting points (for values without references see [148]).

No.	Equilibrium	ΔH^0(298) [kcal/mol]	ΔS^0(298) [cal/K·mol]	ΔC_p estimated [cal/K·mol]	Ref.	ΔH^0(melt) at m.p. [kcal/mol]
1	$MgCl_{2,s} + Al_2Cl_{6,g} \rightleftharpoons MgAl_2Cl_{8,g}$	11	11	−1.5	[15]	10.3
2	$CaCl_{2,s} + Al_2Cl_{6,g} \rightleftharpoons CaAl_2Cl_{8,g}$	13	11	−1	[15]	6.8
3	$CrCl_{2,s} + Al_2Cl_{6,g} \rightleftharpoons CrAl_2Cl_{8,g}$	10	12	−1	[128]	7.7
4	$MnCl_{2,s} + Al_2Cl_{6,g} \rightleftharpoons MnAl_2Cl_{8,g}$	11	11	−1	[15]	9.0
5	$CoCl_{2,s} + Al_2Cl_{6,g} \rightleftharpoons CoAl_2Cl_{8,g}$	11	10	−1	[15, 132—135]	14.1
6	$NiCl_{2,s} + Al_2Cl_{6,g} \rightleftharpoons NiAl_2Cl_{8,g}$	13	11	−1	[15]	18.5
7	$CuCl_{2,s} + Al_2Cl_{6,g} \rightleftharpoons CuAl_2Cl_{8,g}$	7	9		[136]	
8	$PdCl_{2,s} + Al_2Cl_{6,g} \rightleftharpoons PdAl_2Cl_{8,g}$	8	10	−1	[130]	11.5
9	$PtCl_{2,s} + Al_2Cl_{6,g} \rightleftharpoons PtAl_2Cl_{8,g}$	7	8	−1	[131]	
10	$MnCl_{2,s} + Fe_2Cl_{6,g} \rightleftharpoons MnFe_2Cl_{8,g}$	13	10	−1	[15]	9.0
11	$CoCl_{2,s} + Fe_2Cl_{6,g} \rightleftharpoons CoFe_2Cl_{8,g}$	13	10	−1	[15]	14.1
12	$NiCl_{2,s} + Fe_2Cl_{6,g} \rightleftharpoons NiFe_2Cl_{8,g}$	15	10	−1	[15]	18.5
13	$CdCl_{2,s} + Fe_2Cl_{6,g} \rightleftharpoons CdFe_2Cl_{8,g}$	13	10	−1	[15]	7.2
14	$UCl_{4,s} + Al_2Cl_{6,g} \rightleftharpoons UAl_2Cl_{10,g}$	11	10	−3	[19]	10.7
15	$NdCl_{3,s} + 1.5\,Al_2Cl_{6,g} \rightleftharpoons NdAl_3Cl_{12,g}$	11	2	0	[144]	12.0
16	$ThCl_{4,s} + Tl_2Cl_{2,g} \rightleftharpoons Tl_2ThCl_{6,g}$	14			[7, 47, 99]	10.5 [149]; 14.7 [150]
17	$UCl_{4,s} + Tl_2Cl_{2,g} \rightleftharpoons Tl_2UCl_{6,g}$	9			[47]	10.7

[a] For further data on the formation of complexes $CuAl_2Cl_8$, $CoGa_2Cl_8$, $MgFe_2Cl_8$, $CaFe_2Cl_8$, $SrFe_2Cl_8$, $BaFeCl_8$, and $GdFe_3Cl_{12}$ see [135].

Compounds with formulas that differ from the previously assumed "basic types" are collected, together with their thermodynamic data, in Table 12.

Here too complex formations are weakly endothermic, as are those formulated in Table 11. However, considerable uncertainty attaches to most of the values given in Table 12, for which the complexity of the systems concerned is partly respon-

Table 12. Thermodynamic data for complexes that do not correspond to the fundamental types.

No.	Equilibrium	ΔH^0(298) [kcal/mol]	ΔS^0(298) [cal/K·mol]	ΔC_p estimated [cal/K·mol]	Ref.
1	$MgCl_{2,s} + 1.5\,Al_2Cl_{6,g} \rightleftharpoons Mg(AlCl_4)(Al_2Cl_7)_g$	−0.1	−6.5	1	[15]
2	$CaCl_{2,s} + 1.5\,Al_2Cl_{6,g} \rightleftharpoons Ca(AlCl_4)(Al_2Cl_7)_g$	11.5	7.3	1	[15]
3	$VCl_{2,s} + 1.5\,Al_2Cl_{6,g} \rightleftharpoons V(AlCl_4)(Al_2Cl_7)_g$	4.1	−7.0	1	[101]
4	$MnCl_{2,s} + 1.5\,Al_2Cl_{6,g} \rightleftharpoons Mn(AlCl_4)(Al_2Cl_7)_g$	9.2	6.9	1	[15]
5	$CoCl_{2,s} + 1.5\,Al_2Cl_{6,g} \rightleftharpoons Co(AlCl_4)(Al_2Cl_7)_g$	6.2	2.0	1	[15]
6	$CoCl_{2,s} + 2\,Al_2Cl_{6,g} \rightleftharpoons Co(Al_2Cl_7)_{2,g}$	11.9	9.1	3	[133]
7	$CoCl_{2,s} + 2\,Al_2Cl_{6,g} \rightleftharpoons Co(Al_2Cl_7)_{2,g}$	10.5	5.5	3	[15, 133]
8	$NdCl_{3,s} + 2\,Al_2Cl_{6,g} \rightleftharpoons Nd(AlCl_4)_2(Al_2Cl_7)_g$	0	−16.1	3.5	[144]
9	$VCl_{3,s} + Al_2Cl_{6,g} \rightleftharpoons VCl(AlCl_4)_{2,g}$	13.3	7.3	−0.5	[101]

sible; also, some of the formulas are not yet fully proved. For example, the measurements in the system $CoCl_2/Al_2Cl_6$ can be evaluated in a form that allows $CoAl_3Cl_{11}$ or $CoAl_4Cl_{14}$ to be present alongside the strongly dominant complex $CoAl_2Cl_8$[113]; probably, indeed, all three complexes are present together. The uncertainty of the data arises from the large entropy differences between reactions of the same type (Table 12, Nos. 1 to 5). Critical examination of the reaction entropies, elsewhere so informative, does not at once lead to progress since there are no reliable ΔS^0 values for large gaseous complexes. The loss of translational entropy on the formation of complexes containing Al_2Cl_7 ligands is clearly almost compensated by the large vibrational entropy of the mainly ionic and thus easily deformable complexes. Without such an effect the measurable concentration of complexes containing Al_2Cl_7 ligands would be difficult to understand, for the ΔH^0 term should not be decisive for the formation of the larger complex for reasons of coordination. The data from *Dell'Anna* and *Emmenegger*[133] for eq. (20) point in the same direction:

$$Co(AlCl_4)_{2,g} + Al_2Cl_{6,g} \rightleftharpoons Co(Al_2Cl_7)_{2,g}; \quad \Delta H^0 = 3\,\text{kcal}; \quad \Delta S^0 = 2\,\text{cal/K} \qquad (20)$$

6. Several Complexes in Equilibrium with One Another

The coexistence of several complexes in equilibrium systems should in principle be expected. For the systems considered in this review the probability attaching to such coexistence of differing gaseous complexes is increased because of the predominantly ionic and thus unspecific bonding forces. This raises for each such system the questions whether the complex described is accompanied by other observable complexes, and to what extent the presence of these other observable complexes may have falsified the thermodynamic data determined for the "main" complex. Answering these questions runs into experimental difficulties, and the same is true for mass spectrometry which usually provides so much information but where large hetero-complexes composed of chlorides could undergo far-reaching fragmentation.

6.1. Systems Not Containing Alkali Metals

For coexistence of complexes containing $AlCl_4$ and Al_2Cl_7 groups, *e.g.* $CoAl_2Cl_8$, $CoAl_3Cl_{11}$, and $CoAl_4Cl_{14}$ see Section 5.2. The unknown 1:1 complex $CoAlCl_5$ could—as estimates have shown[108]—have only slight importance in comparison with $CoAl_2Cl_8$.

For *combinations containing TlCl, CuCl, or InCl₃* there are quantitative data [eq. (21) to (37)][47].

$$TlCl_g + InCl_{3,g} \rightleftharpoons TlInCl_{4,g}; \quad \Delta H^0 = -27.9\,\text{kcal} \qquad (21)$$
$$2TlCl_g + InCl_{3,g} \rightleftharpoons Tl_2InCl_{5,g}; \quad \Delta H^0 = -50.0\,\text{kcal} \qquad (22)$$

Here there is an uncertainty, since the fragment $Tl_2InCl_4^+$ observed in the mass spectrometer was ascribed to Tl_2InCl_5. In complexes *containing alkali metals*—which however are a special case—the fragments $A_2MCl_4^+$ are derived mainly from $A_2M_2Cl_8$.

$$CuCl_g + ThCl_{4,g} \rightleftharpoons CuThCl_{5,g}; \quad \Delta H^0 = -46.3\,\text{kcal} \qquad (23)$$
$$2CuCl_g + ThCl_{4,g} \rightleftharpoons Cu_2ThCl_{6,g}; \quad \Delta H^0 = -100.2\,\text{kcal} \qquad (24)$$
$$CuCl_g + 2ThCl_{4,g} \rightleftharpoons CuTh_2Cl_{9,g}; \quad \Delta H^0 = -80.9\,\text{kcal} \qquad (25)$$

$$TlCl_g + ThCl_{4,g} \rightleftharpoons TlThCl_{5,g}; \quad \Delta H^0 = -27.3\,\text{kcal} \qquad (26)$$
$$2TlCl_g + ThCl_{4,g} \rightleftharpoons Tl_2ThCl_{6,g}; \quad \Delta H^0 = -64.1\,\text{kcal} \qquad (27)$$

$$CuCl_g + UCl_{4,g} \rightleftharpoons CuUCl_{5,g}; \quad \Delta H^0 = -46.7\,\text{kcal} \qquad (28)$$
$$2CuCl_g + UCl_{4,g} \rightleftharpoons Cu_2UCl_{6,g}; \quad \Delta H^0 = -101.6\,\text{kcal} \qquad (29)$$

$$TlCl_g + UCl_{4,g} \rightleftharpoons TlUCl_{5,g}; \quad \Delta H^0 = -29.2\,\text{kcal} \qquad (30)$$
$$2TlCl_g + UCl_{4,g} \rightleftharpoons Tl_2UCl_{6,g}; \quad \Delta H^0 = -65.6\,\text{kcal} \qquad (31)$$
$$TlCl_g + 2UCl_{4,g} \rightleftharpoons TlU_2Cl_{9,g}; \quad \Delta H^0 = -58.4\,\text{kcal} \qquad (32)$$

$$BeCl_{2,g} + InCl_{3,g} \rightleftharpoons BeInCl_{5,g}; \quad \Delta H^0 = -25.0\,\text{kcal} \qquad (33)$$
$$2BeCl_{2,g} + InCl_{3,g} \rightleftharpoons Be_2InCl_{7,g}; \quad \Delta H^0 = -53.0\,\text{kcal} \qquad (34)$$
$$3BeCl_{2,g} + InCl_{3,g} \rightleftharpoons Be_3InCl_{9,g}; \quad \Delta H^0 = -80.2\,\text{kcal} \qquad (35)$$

$$ZnCl_{2,g} + InCl_{3,g} \rightleftharpoons ZnInCl_{5,g}; \quad \Delta H^0 = -24.6\,\text{kcal} \qquad (36)$$
$$SnCl_{2,g} + InCl_{3,g} \rightleftharpoons SnInCl_{5,g}; \quad \Delta H^0 = -24.5\,\text{kcal} \qquad (37)$$

These reaction enthalpies, derived from mass spectra, have limits of error of approximately ± 2 kcal. Critical examination leads to the following conclusions:

a) On 1:1 addition of M'Cl to MCl_x the ΔH^0 is roughly half as large as for 2:1 addition.

b) Statement a) can be refined by noting that C.N.=4 ($TlInCl_4$) or 6 (Cu_2ThCl_6; Tl_2ThCl_6; Cu_2UCl_6; Tl_2UCl_6) for M is distinctly favored over C.N.=5, as shown by the ΔH^0 values.

c) If in larger complexes identical central atoms M are linked by Cl bridges, their formation in the sense of eq. (38) to (44) is energetically comparable with dimerization of MCl_x, and the effect of coordination number is again evident.

$$ThCl_{4,g} + ThCl_{4,g} \rightleftharpoons Th_2Cl_{8,g}; \quad \Delta H^0 = -31.0\,\text{kcal} \qquad (38)$$
$$CuThCl_{5,g} + ThCl_{4,g} \rightleftharpoons CuTh_2Cl_{9,g}; \quad \Delta H^0 = -34.6\,\text{kcal} \qquad (39)$$

$$UCl_{4,g} + UCl_{4,g} \rightleftharpoons U_2Cl_{8,g}; \quad \Delta H^0 = -26.1\,\text{kcal} \qquad (40)$$
$$TlUCl_{5,g} + UCl_{4,g} \rightleftharpoons TlU_2Cl_{9,g}; \quad \Delta H^0 = -29.2\,\text{kcal} \qquad (41)$$

$$BeCl_{2,g} + BeCl_{2,g} \rightleftharpoons Be_2Cl_{4,g}; \quad \Delta H^0 = -24.0\,\text{kcal} \qquad (42)$$
$$BeInCl_{5,g} + BeCl_{2,g} \rightleftharpoons Be_2InCl_{7,g}; \quad \Delta H^0 = -28.0\,\text{kcal} \qquad (43)$$
$$Be_2InCl_{7,g} + BeCl_{2,g} \rightleftharpoons Be_3InCl_{9,g}; \quad \Delta H^0 = -27.2\,\text{kcal} \qquad (44)$$

d) Complexes containing CuCl are characterized by particularly great stability, and the same may be the case for AgCl complexes. This is explained by the high aggregation enthalpy of the monochloride.

6.2. Systems Containing Alkali Metals

In larger hetero-complexes containing two alkali-metal atoms as well as the metal atom M, the alkali-metal atoms have a positive partial charge owing to their low electronegativity. This effect is increased in the positively charged molecular ion that arises primarily by electron impact. Further fragmentation is prescribed by such a charge profile. It leads mainly or exclusively to fragment ions that contain the A atoms but are impoverished in M, and whose origin is not immediately evident. Tracing the fragments back to the initial complex requires additional studies that have not yet been done for chloride complexes. For *fluoride* complexes, however, *Sidorov et al.* in particular have developed methods for decoding the mass spectra of equilibrium systems of several complexes con-

taining alkali-metals[152]. Examples of gaseous complexes observed in this way are:

NaF/BeF_2 system: $NaBeF_3$, Na_2BeF_4, $(NaBeF_3)_2$ [153]
KF/AlF_3 system: $KAlF_4$, K_2AlF_5, $(KAlF_4)_2$ [154]
NaF/GaF_3 system: $NaGaF_4$, Na_2GaF_5, $(NaGaF_4)_2$ [155]

Chloride systems apparently behave analogously, so that a certain amount of order becomes recognizable in the build-up of such equilibrium systems.

ACl/MCl_2: With this combination the fragment $AMCl_2^+$ is generally observed in the mass spectrometer, and can be unambiguously ascribed to the $AMCl_3$ molecule. When A = K, and M = Mn, Fe, Co, Ni or Pb, the fragment $A_2MCl_3^+$ is also observed[156], this indicating the existence of a further complex A_2MCl_4 or $(AMCl_3)_2$.

ACl/MCl_3: In the systems $KCl/AlCl_3$ and $ACl/GaCl_3$ (A = Na, K, Rb, Cs) the fragment $AMCl_3^+$ derived from $AMCl_4$ was observed mass-spectrometrically together with $A_2MCl_4^+$, which is formed from A_2MCl_5 or $(AMCl_4)_2$[156].

7. Practical Significance of Gaseous Complexes

General considerations: Gaseous complexes formed from halide molecules are labile in the kinetic sense. The components AX_m and BX_n bound in the complex are available for further reaction without kinetic hindrance provided that the thermo-

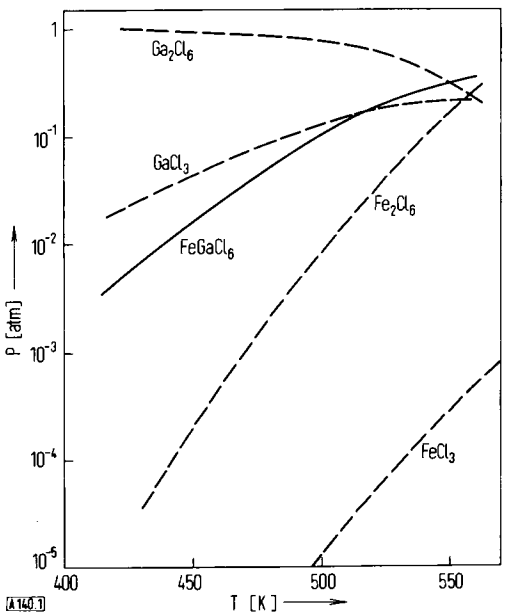


Fig. 1. Equilibrium pressures above solid iron(III) chloride in the presence of gallium (III) chlorides at $\Sigma P = 1$ atm.

dynamics demand it. The situation is particularly clear when one investigates whether a given equilibrium system is altered by addition of one of the components of the complex. Examples of this are shown in Figures 1 to 4.

Figure 1 makes it clear that the addition of a large excess of the readily volatile component $GaCl_3$ (Ga_2Cl_6) of the complex causes an appreciable increase in the total Fe content of the gas phase, although the stability of the complex is low, as shown by the fact that $\log K_P = 0$ for the reaction

$$\tfrac{1}{2}\,Fe_2Cl_{6,g} + \tfrac{1}{2}\,Ga_2Cl_{6,g} \rightleftharpoons FeGaCl_{6,g} \qquad (45)$$

(see Section 4).

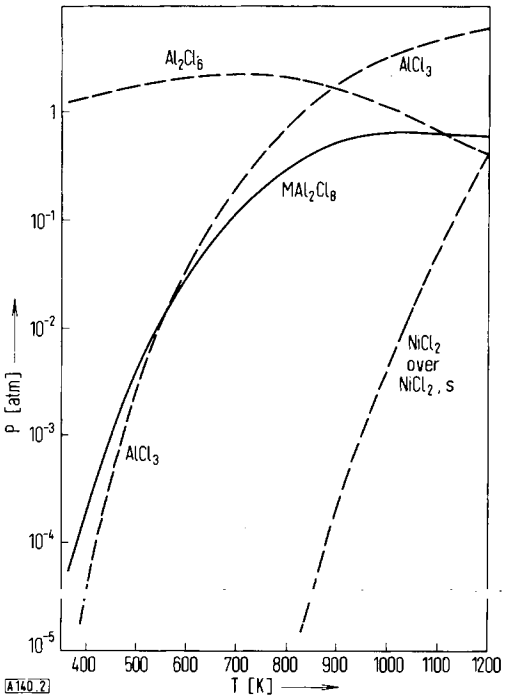


Fig. 2. Equilibrium pressures above solid nickel(II) chloride for the case in which the reaction space is filled at 293 K with Al_2Cl_6 at a (hypothetical) partial pressure of 1 atm.

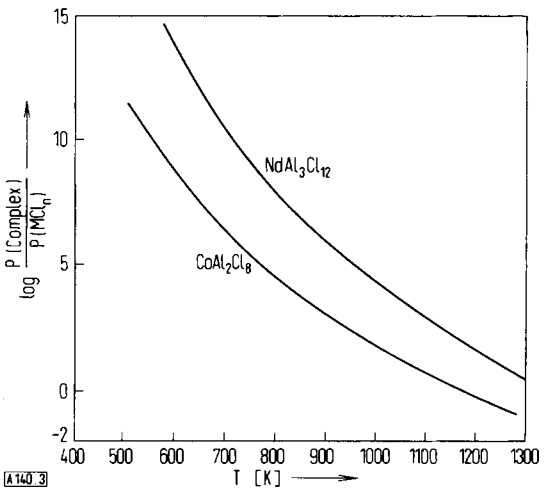


Fig. 3. Comparison of the saturation pressures above solid $CoCl_2$ and $NdCl_3$ with equilibrium pressures of the $AlCl_3$ complexes. Filling of the reaction space as in Figure 2.

It is also important that the relevant concentrations of the complexes decrease with rising temperature and that there is an upper temperature limit above which complex formation can be neglected for practical purposes because the uncomplexed components strongly predominate (cf. Figures 1—4 and [157]).

Table 13 provides a survey of the large number of complex-forming systems with the single important requirement that one of the readily volatile trichlorides $AlCl_3$, $GaCl_3$, $InCl_3$, or $FeCl_3$ shall function as complex-former[108].

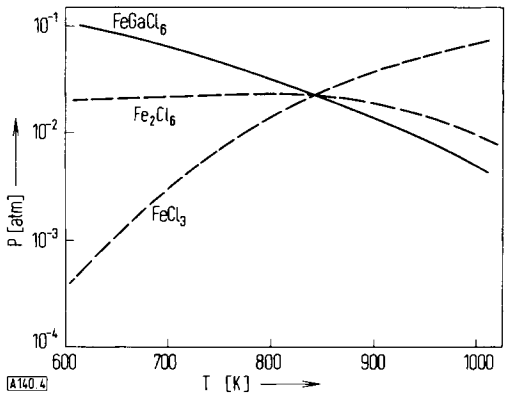


Fig. 4. Equilibrium pressures of the Fe-containing molecules above α-Fe_2O_3 as the bottom material, as set up in the presence of HCl and $GaCl_3$ (Ga_2Cl_6) when $\Sigma P = 4$ atm and $Ga/H = 1$. $Ga/H = [P(GaCl_3) + 2P(Ga_2Cl_6) + P(FeGaCl_6)] : [P(HCl) + 2P(H_2O)]$.

Finally we show by examples that the family of gaseous complexes also deserves interest from the practical point of view.

Gaseous complexes in preparative chemistry: Relatively slightly volatile halides (*e.g.* $TiCl_3$, VCl_3, $CrCl_3$, $MnCl_2$, $FeCl_2$, $CoCl_2$, $NiCl_2$, $CuCl_2$, $ScCl_3$, YCl_3, $LaCl_3$, $ThCl_4$, UCl_4) can be transported chemically through temperature gradients by means of readily volatilized complex-formers ($AlCl_3$, $GaCl_3$, $InCl_3$, or $FeCl_3$) and can thus be obtained crystalline at much lower temperatures than can be used for their sublimation[96]. The combination of this chemical transport, which takes care of the mobility of the components, together with other reactions, leads to new synthetic routes, *e.g.* for $CrCl_2$[129], Pd_2Al[89] and $HgCr_2Se_4$[96]. Other references to this type of problem have been collected by *Emmenegger*[157]. The separation of lanthanoids and actinoids by gas chromatography of the aluminum chloride complexes[138,139] is also worth noting.

Gaseous complexes in industrial problems: When studying the electrolytic separation of aluminum from melts containing $AlCl_3$[158], *Grothe*[10] observed that alkali-metal chlorides—and also magnesium chloride—were volatilized in considerable quantities with aluminum chloride, being carried away in the gas released at the anode. The gaseous fluoride complex $NaAlF_4$ plays a similar part in the usual industrial extraction of aluminum[159]. *Dewing*[15] noted the volatilization of $MgCl_2$ and $CaCl_2$ with the formation of $AlCl_3$ complexes in connection with the studies of the "aluminum(I) chloride process" (isolation of Al by chemical transport by the reversible reaction $2Al_l + AlCl_{3,g} \rightleftharpoons 3AlCl_g$).

In the isolation of copper from copper ores the so-called "segregation process" has proved valuable[72]. In this the oxidic copper ore is heated in the presence of NaCl, SiO_2, C, and H_2O_g. The HCl first produced leads to the formation of $Cu_3Cl_{3,g}$, which is finally reduced by the H_2 and deposited on the carbon-containing granules. According to *Gross* and *Stuart*'s thermodynamic investigation of the process[72], this scheme needs supplementation in that a NaCl/CuCl melt is formed as an intermediate stage and that in the subsequent step not only $Cu_3Cl_{3,g}$ but also the gaseous complexes $NaCuCl_2$ and $NaCu_2Cl_3$ play a considerable role in transporting the copper onto the carbon.

In the treatment of sulfidic copper ores with chlorine with the aim of converting the copper into water-soluble $CuCl_2$ and at the same time volatilizing the chlorides of sulfur and iron, *Spreckelmeyer*[160] found that appreciable volatilization of $CuCl_2$ began when the iron content ($FeCl_3$) was high. The explanation for this is provided by the existence of the gaseous complex $CuFe_2Cl_8$, whose reversible formation has been observed during chemical transport of $CuCl_2$ with $FeCl_3$ (Fe_2Cl_6)[96].

Gaseous complexes in high-pressure discharge tubes: Discharge tubes filled with mercury, which also contain argon as the ignition gas, are important because of their high light output. Their further development, with the object of improving the light yield and achieving a radiation similar to daylight, requires the inclusion also of other elements whose atoms can be excited in the plasma column (*ca.* 6000 K). The content of such elements in the gas space is limited by their saturation pressure at the temperature of the tube wall (*ca.* 1000 K). This threshold can be passed if halides are used in place of the elements. The halides are decomposed in the plasma and re-formed near the wall. The more deciding factor is now the saturation pressure of the halides at the wall. This pressure is still lower than desired when particularly efficient radiators such as scandium or the lanthanoids are used, and thus complex formers have been added to produce more easily volatilized gaseous complexes such as AMI_4; examples are $ScI_3 + NaI$[161] and $CeI_3 + NaI + CsI$[162–164]. Iodides are favored for this purpose because, in contrast to the analogous chloride systems, they do not lead to attack on the tungsten electrodes (by the free halogen).

Table 13. Elements whose chlorides form gaseous complexes with $AlCl_3$ (or $GaCl_3$, $InCl_3$ or $FeCl_3$). Bold type denotes that the formation of a gaseous complex has been proved. Parentheses denote that such complex formation can be safely assumed, but that this has not yet been investigated.

Li	**Be**												B	C	N	O	F
Na	**Mg**					**Cr^{III}**		**Fe^{III}**				**Cu^{I}**		**Al**	Si	P	S	Cl
	K	**Ca**	**Sc**	**Ti^{III}**	**V**	**Cr^{II}**	**Mn^{II}**	**Fe^{II}**	**Co**	**Ni**	**Cu^{II}**	**Zn**	**Ga**	Ge	As	Se	Br
	Rb	**Sr**	**Y**	**(Zr)**	**Nb**	**Mo**	Tc	**Ru**	**Rh**	**Pd**	**Ag**	**Cd**	**In**	**Sn^{II}**	**Sb**	Te	I
	Cs	**Ba**	**La**	**(Hf)**	**(Ta)**	W	Re	Os	**Ir**	**Pt**	**Au^{III}**	**Hg^{II}**	**Tl**	**Pb**	**Bi^{I}** Bi^{III}	Po	At
			Ce	**Pr**	**Nd**	**Pm**	**(Sm)**	**Eu**	**Gd**	**Tb**	**Dy**	**(Ho)**	**(Er)**	**Tm**	**Yb**	**Lu**	
			Th	Pa	**$U^{III,IV,V}$**	Np	**Pu**	**Am**	**Cm**								

Gaseous complexes in high-pressure discharge tubes: Discharge tubes filled with mercury, which also contain argon as the ignition gas, are important because of their high light output. Their further development, with the object of improving the light yield and achieving a radiation similar to daylight, requires the inclusion also of other elements whose atoms can be excited in the plasma column (*ca.* 6000 K). The content of such elements in the gas space is limited by their saturation pressure at the temperature of the tube wall (*ca.* 1000 K). This threshold can be passed if halides are used in place of the elements. The halides are decomposed in the plasma and re-formed near the wall. The more deciding factor is now the saturation pressure of the halides at the wall. This pressure is still lower than desired when particularly efficient radiators such as scandium or the lanthanoids are used, and thus complex formers have been added to produce more easily volatilized gaseous complexes such as AMI_4; examples are $ScI_3 + NaI$[161] and $CeI_3 + NaI + CsI$[162–164]. Iodides are favored for this purpose because, in contrast to the analogous chloride systems, they do not lead to attack on the tungsten electrodes (by the free halogen).

It may be expected that further information about the practical utilization of gaseous complexes will soon appear. In this connection one might bear in mind, for example, the removal of impurities as well as their fixation (masking) in the form of gas complexes during the preparation of doped or very pure materials.

8. Unanswered Questions

The chemistry of gaseous complexes has now been clarified to an extent that allows the principal problems still awaiting

solution to be named. In the author's opinion these are the following:

1) *Thermodynamics*

a) The basis for estimating the stability of 1:1 hetero-complexes, and particularly of complexes containing alkali metals, should be broadened by reliable measurements. The object of this would be to systematize the *Y* values.

b) The analogy of the *chloride* complexes to those of *fluorides*, *bromides*, and *iodides* is obvious. It would be important and useful to discover quantitative relationships between the various halide complexes.

c) The approximation formulas and rules customarily used today for estimating normal entropies were developed for small molecules. They fail for very large, ionic, gaseous complexes. In these complexes energetically low, easily excited, vibrations clearly lead to unusually large entropy values. Quantitative investigations in this area are needed. Promising routes would be exploration of the IR and Raman spectra of gaseous complexes condensed in a matrix.

d) A special problem is presented by the existence of equilibrium systems containing several complexes (cf. Section 6). Even analysis of such mixtures is difficult. After a sufficiently wide experimental basis has been worked out, the numerical material obtained should be examined for systematic relationships.

2) *Structures*

The structural concepts so far reached are, with few exceptions, based on ligand field spectra. In these admittedly the coordination of only the cation providing the color is determined. The capacity of other methods of investigation to provide information is often diminished by the complicated composition of the equilibrium gas. In this area too vibration spectroscopy with matrix isolation could help matters forward.

3. In *preparative investigations* the existence of gaseous complexes and their application should be taken more seriously into account. Some of the complexes existing in the gas phase can, according to our observations, also be obtained in apolar or weakly polar solvents. Studies in this direction must be continued. They could open up the possibility of new reactions, particularly for compounds of the transition elements.

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Is Gold Chemistry a Topical Field of Study?

By Hubert Schmidbaur[*]

The question raised in the title of this progress report is answered point for point with an emphatic "yes": Ranging from metallic gold, *via* clusters of gold atoms in low valence states, compounds of Au^{I}, Au^{II}, Au^{III}, and Au^{V}, organogold derivatives, ylide and carbene complexes, to the catalytic activity of gold it embraces a long-neglected area of chemistry holding promise of many a discovery.

1. Introduction

1.1. Historical

Metallic gold has from antiquity been regarded as the very epitome of material value. The continuing practice of striking coins in this metal (if not as legal currency, then as an inflation hedge and a speculative form of investment), the still at least partly valid relation between actual currencies and national gold reserves (Fort Knox!), and finally the undisputed preference for gold as the basic material of jewelry are an obvious reason for and a clear manifestation of this idea. The idea therefore grew up not only among laymen, but also among chemists, that gold should be ascribed a special place among the elements. It is not uncommon to encounter the prejudice that occupation with gold *chemistry* reveals an inability to grasp reality since the use of gold for purposes other than those mentioned above is inconceivable. The question of "relevance" is therefore best disregarded in this context.

Continuing in this vein, a general survey of the principal combinations of the element does indeed show that in most chemical systems elemental gold is distinctly favored thermodynamically over its compounds[1]. Nature itself has predestined gold's role as a noble metal in the truest sense of the word. Thus apart from its combinations with strongly oxidizing halogens, gold chemistry is a chemistry of metastable compounds and leads almost invariably—whether desired or not—to elemental gold as the essentially stable species. With few exceptions the metal also occurs as elemental gold in its natural deposits[1].

1.2. The Present Situation

Such a standpoint nevertheless overlooks a number of aspects which present this neglected area of inorganic and organometallic chemistry in a much more favorable light. It should first be mentioned that the price of gold is currently much lower than that of many so-called "rare" metals. For instance, platinum, palladium, iridium, rhodium, osmium, and ruthenium are traded at a price much higher than that of gold. Yet these metals and their compounds are frequently utilized in practice and are still under intensive study. Moreover, gold is on no account one of the rarest elements and its abundance far exceeds that of most of the above noble metals. Its scarcity may therefore merely be a result of hoarding reserves.

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In addition the *uses* of gold are no longer restricted to coinage and jewelry, but are steadily increasing in number and scope. An example that has received considerable publicity through spectacular photographs is the coating of aerospace equipment with a bright gold plating; and another one is the gold coating of radiation-inhibiting window panes characterizing the appearance of numerous modern buildings. Gold is also used in collectors for solar energy and is predicted to have a great future in that field.

Even more manifold but less evident to the casual observer is the role of gold in the microcosm of the latest generation of electronic equipment; many components and circuits would be unthinkable without gold.

An old rule of *catalyst* research appears to regard gold as a black sheep among the noble metals, for it has so far found practically no catalytic application. The activity of the neighboring elements platinum and palladium underlines this shortcoming. However, recent findings suggest that these ideas may soon be due for revision.

Finally, mention should be made of the use of gold in *medicine* and *dentistry*. Although many attempts have been made to develop new methods for treating polyarthritis, the classical field of application of gold therapy, we still cannot dispense with this "chrysotherapy". It remains a topic for research to discover gold compounds in which therapeutic action and heavy metal toxicity are related as favorably as possible[2].

This brief survey should demonstrate that research into gold chemistry often has a very realistic basis. Most of the new working forms of gold are obtained *via* gold compounds, and a deepening of our understanding of their chemistry is therefore highly desirable.

An attempt is made in the following to trace advances and developmental trends with the aid of important contributions to gold chemistry dating from the past five years, and to stimulate further study of this most enchanting material. No claim can be made to completeness, and the choice is necessarily subjective. *Organogold compounds* are treated separately (Section 7), an approach justified by the unparalleled development of this field of gold chemistry[3]. This promotes clearer understanding by providing an opportunity for a more detailed examination of various aspects.

2. Elemental Gold and Clusters of Gold Atoms in Low Valence States

2.1. Gold Vapor and Gold Metal

The three states of aggregation of elemental gold were studied in considerable detail at a very early stage[1]. A very remarkable

result is that, above the boiling point of the metal, gold vapor consists primarily of dimers Au_2 characterized by one of the largest dissociation energies known for homonuclear diatomic molecules[4]. The experimental value $E_D = 232$ kJ/mol exceeds the dissociation energy of almost all halogens and interhalogen compounds of type A_2 and AB.

There has therefore been no lack of attempts[5-7] to trap the Au_2 species by complex formation; simple donors should give products *(1a)* isoelectronic with the mercury(I) compounds *(1b)*:

$$\text{Au–Metal} \xrightarrow{\Delta} \text{Au–Au} + 2\ \text{:L} \longrightarrow \text{L–Au–Au–L} \quad (1a)$$

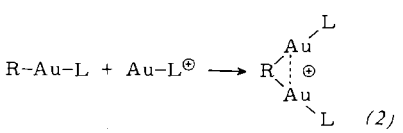
$$\text{Hg–Hg}^{2\oplus} + 2\ \text{:X}^{\ominus} \longrightarrow \text{X–Hg–Hg–X} \quad (1b)$$

The ligands L tried were mainly phosphanes R_3P or sulfanes R_2S. Astonishingly, not a single complex *(1a)* has yet been isolated, or even detected. The same applies to reduction experiments on gold compounds in solution, which have long been known to afford a large variety of gold colloids[1]. However, the occurrence of discrete, well-defined polyatomic aggregates, *i.e.* clusters, has recently been detected. The metallic nuclei of these clusters which are enclosed by a sheath of ligands may be regarded as a link between the particles found in the metal vapor and the practically infinite aggregates of the molten and the crystalline metal. No other metal has yet been found to form as many different homoatomic clusters as gold. A knowledge of the structure of such species can provide valuable information pertaining to metal nuclei, their formation and their growth[5].

2.2. Gold Clusters

Metallic gold crystallizes in a cubic face-centered lattice, with each metal atom being surrounded by 12 equidistant neighbors (Au—Au distance 288.4 pm). The mechanical and electrical properties of this soft, readily workable metal having good electrical and thermal conductivity can be attributed principally to this lattice type (m.p. 1064.43 °C, b.p. 2860 °C).

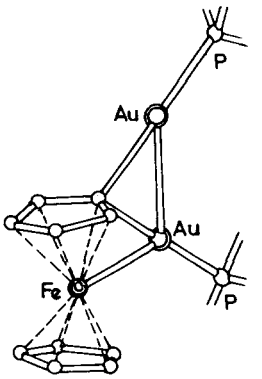
The smallest metal aggregate containing two atoms in a low oxidation state (<1), the Au_2 unit, was first discovered by *Nesmeyanov et al.* in organogold compounds of type *(2)*[8]. However, this is not the simple unbridged form [cf. *(1a)*], but the triatomic CAu_2 structural unit in which a tetrahedrally coordinated C atom serves as a bridge between two gold atoms in direct contact. Such species are formed on reaction of RAuL complexes with $AuL^{\oplus}$ ions:



(2)

R is initially a triply coordinated C atom of an aromatic or olefinic group which achieves the coordination number 4 in the course of the reaction: $R = C_6H_5$, $C_6H_4CH_3$, $CH_2{=}CH$, ferrocenyl (Fc), *etc.* The last-named example [*(3)*] has been confirmed by an X-ray study[9].

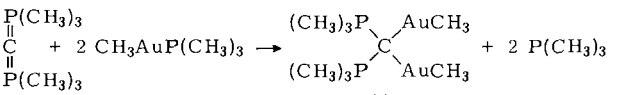
The Au—Au distance is 277 pm and is thus shorter than in metallic gold. (Compounds containing $Au_2^{4\oplus}$ units will be considered in Section 4.)



$[Fc\{AuP(C_6H_5)_3\}_2]^{\oplus}\ BF_4^{\ominus}$

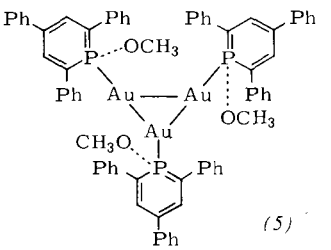
(3)

Compounds have also been found in which two gold atoms *not* linked together are bonded to the same C atom. While a first series of examples[8] closely resemble those of type *(2)*, a second class can be derived from the carbodiphosphoranes $R_3P{=}C{=}PR_3$[10]. The latter readily form 1 : 2 complexes with gold(I) reactants, according to



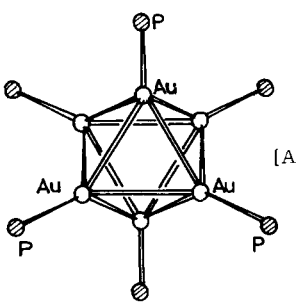
(4)

Dimroth et al.[11] recently postulated a structure containing an Au_3 unit for a compound formed on reaction of the AuCl complex of 2,4,6-triphenyl-λ^3-phosphorin[12] with sodium methoxide. Determination of the relative molecular mass indicated the trimer, and spectroscopic data accord with structure *(5)*.



(5)

The next larger cluster unit, a Au_6 octahedron, was first discovered in the group of gold compounds studied in great detail by *Malatesta et al.* during recent years[13]. They were prepared by careful reduction of phosphane complexes LAuX (X = (pseudo)halogen, L = phosphane) and the products isolated by employing special crystallization techniques. Some of the products have the composition $[Au_6L_6]^{2\oplus} + 2X^{\ominus}$, thus implying a formal oxidation state of +0.33 for the gold atoms.

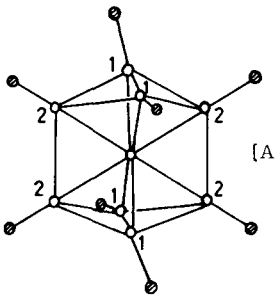


$[Au_6\{P(p\text{-}C_6H_4CH_3)_3\}_6]^{2\oplus} \cdot 2\ [B(C_6H_5)_4]^{\ominus}$

(6a)

The structure was determined by X-ray analysis on *(6a)*. The Au—Au distance of *ca.* 300 pm in the cation is longer than in metallic gold!

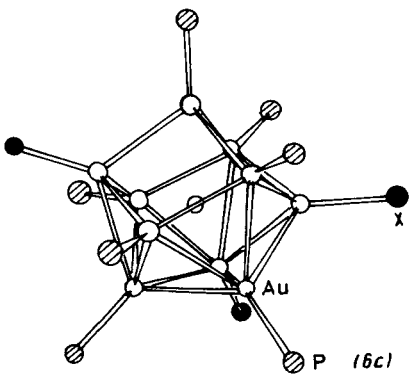
The same reduction, usually carried out (like many processes yielding gold colloids) with alkali tetrahydridoborates, affords products of composition $[Au_9L_8]^{3\oplus}\cdot 3X^{\ominus}$ as a further type of cluster. Once again the gold can be assigned an average oxidation state (+0.33), but structure *(6b)* shows one of the metal atoms to occupy a distinctive central position. The metal nucleation is clearly appreciated, even though the coordination is initially only 8. The Au—Au distance (*ca.* 276 pm) is already approaching that in the metal[14].



$[Au_9\{P(p\text{-}C_6H_4CH_3)_3\}_8]^{3\oplus}\cdot 3\ [PF_6]^{\ominus}$

(6b)

In clusters of formula $[Au_{11}L_7]^{3\oplus}\cdot 3X^{\ominus}$ a coordination number of 10 is achieved[15a], with Au—Au distances of *ca.* 270 (central) and 290 pm (peripheral) and an average oxidation number of only +0.27. The nucleation in *(6c)* has therefore almost reached the arrangement in the metal. Knowledge of the precise geometry of the atomic arrangement permits an approximative theoretical treatment of the electronic configuration[15b].



(6c)

The numerous complexes displaying direct contact between the atoms of *gold and other metals* also include clusters, of which those involving Li, Cu, or Zn warrant particular mention. The structures proposed contain metallic units reminiscent of the structural components of alloys[16a,b]:

$Au_2Zn_2(C_6H_5)_6$

$Au_2Li_2[C_6H_4CH_2N(CH_3)_2]_4$

$Au_2Cu_2[C_6H_4CH_2N(CH_3)_2]_4$

Analogous copper and silver compounds are also known[16c].

Discrete gold-transition metal bonds not leading to clusters occur in many carbonyl complexes. The following examples demonstrate that up to three gold atoms can be bonded to a metal center:

$(C_6H_5)_3P\text{–}Au\text{–}Fe(CO)_3NO$[17]

$[(C_6H_5)_3P\text{–}Au]_2Fe(CO)_4$[18]

$[(C_6H_5)_3P\text{–}Au]_3Re(CO)_4$[19]

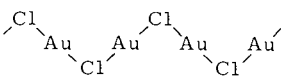
$(C_6H_5)_3P\text{–}Au\text{–}V(CO)_6$[20]

$(C_6H_5)_3P\text{–}Au\text{–}Mn(CO)_4P(OC_6H_5)_3$[21]

3. Compounds of Gold(I)

3.1. Simple Halides and Halo Complexes

Among the gold(I) halides, the chloride, bromide, and iodide have long been known, but only the structure of the last-mentioned halide had been adequately characterized[22]. Only very recently has the crystal structure of AuCl been studied in two laboratories and fully elucidated. X-Ray diffraction analysis of single crystals prepared by chemical transport indicated the angled chain structure, as also occurs in AuI; however, the bond angle at the chlorine is seen to be considerably greater, and the X—Au—X unit is expectedly considerably extended[23]:



Vibrational spectra in the long wave region were reported almost simultaneously which provide more detailed information about force constants and bond orders in gold(I) halides. The hitherto unmeasured bond angle at bromine in AuBr was also predicted[24,25].

Earlier indications for the existence of halo complexes $AuX_2^{\ominus}$ were confirmed by isolation and vibrational spectra of tetraalkylammonium salts such as $[(C_2H_5)_4N]^{\oplus}AuX_2^{\ominus}$, X = Cl, Br, I[26]. The same type of compound was studied in dimethyl sulfoxide solution by electrochemical methods[27]. An example of the X-ray elucidation of the linear triatomic $BrAuBr^{\ominus}$ unit is provided by the structure of bis(di-*n*-butyl-dithiocarbamato)gold(III) dibromoaurate(I)[28]. In contrast, it proved impossible to detect $AuX_2^{\ominus}$ in *molten* gold(I) and alkali halides. Pertinent melt studies of importance for electrochemical gold coating of surfaces resulted in disproportionation[29].

Gold(I) halides are good complexing agents. In recent years attention has been focused mainly on complexes with sulfur and phosphorus donor ligands. However, a facile new synthesis has also been found for the carbonyl complex first prepared over 50 years ago[30]:

$$H_3O^{\oplus}AuCl_4^{\ominus} + 2\ CO \xrightarrow{SOCl_2} 3\ HCl + SO_2 + COCl_2 + Au(CO)Cl$$

Although thermolabile, this carbonyl derivative, which readily dissolves in organic solvents, is a versatile starting material for the synthesis of other Au^I complexes since the CO ligand can be replaced with great ease[31]. The exceptionally short-wave ν(CO) absorption of the compound (2158 cm^{-1}) likewise indicates weak interaction between ligand and metal atom[30,31].

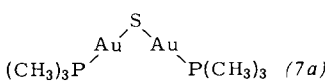
Gold-halogen vibrations were also closely examined specifically on pyridine complexes[32] and constitute an important part of most publications about sulfide and phosphane complexes.

The complex chemistry of gold with pseudohalogens has been surveyed only recently[33,34].

3.2. Sulfur Compounds

Early interest was shown in compounds of sulfur and gold because they were employed for thermal production of gold coatings on ceramics, porcelain, glass, and metal (and later also plastics). This concerns less the pure sulfides than organosulfur derivatives. Incidentally, gold is the only metal not to react directly with sulfur!

Apart from Au_2S, the nature of gold(I) sulfides and thiolates having the formula Au_2S_n and AuSR, respectively, remains largely unelucidated[35,36]. Valuable information has been obtained, though, from some phosphane complexes of these compounds. For instance, a well-defined bis(phosphane) complex of Au_2S *(7a)* is formed from trimethylphosphane-gold chloride and H_2S[37]. Closely related are the complex thiolates *(7b)*—*(7e)*[37–39].



(7a)

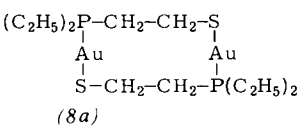
$(CH_3)_3P{-}Au{-}SC_2H_5$ *(7b)*

$(CH_3)_3P{-}Au{-}SC(CH_3)_3$ *(7c)*

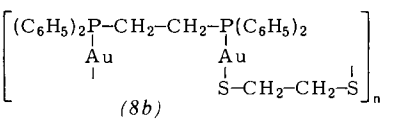
$(C_6H_5)_3P{-}Au{-}SCH_2C_6H_5$ *(7d)*

$(CH_3)_3P{-}Au{-}SCH_2CH_2S{-}Au{-}P(CH_3)_3$ *(7e)*

Compounds having the composition and presumed structure *(8)* have been prepared for therapeutic purposes[40]; *(8a)* has antiarthritic properties.



(8a)



(8b)

Gold(I) salts also form stable complexes with *thioureas*, which, having a ligand ratio of 1:2, are formulated as ionic compounds[41]:

$[(R_2N)_2CS{-}Au{-}SC(NR_2)_2]^{\oplus}X^{\ominus}$ R = H, Alkyl; X = ClO_4, BF_4, CH_3COO

They are of interest for analytical purposes. Analogous bonding has meanwhile been established for the classical *thiosulfate* complex *(9)* by X-ray analysis[42]:

$Na_3[O_3SS{-}Au{-}SSO_3] \cdot 2\,H_2O$ *(9)*

Like the corresponding silver complex, this coordination compound played an important role in the infancy of photography, for which products with gold toning were characteristic[43]. It was also used for treatment of arthritis, tuberculosis, and leprosy[44].

The complex chemistry of the Au^I ion with *thioethers* is extensive, but has so far provided few surprises. Numerous compounds have been characterized by spectroscopy, *e.g.* refs.[45–47]:

$R_2S{-}Au{-}X$ R = CH_3; X = Cl, Br; R = $CH_2C_6H_5$; X = Cl

Such gold complexes are of importance in the extraction of the noble metal[48].

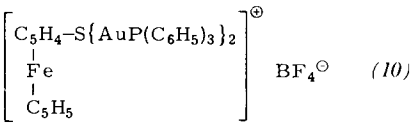
Another series of compounds is derived from *phosphane sulfides* and *selenides:* typical examples are[38,49,50]:

$(C_6H_5)_3PX \cdot AuCl$

$(C_6H_5)_3AsS \cdot AuCl$ X = S, Se

In the *gold/selenium/tellurium* system the new phases AuSe and Au_2SeTe were discovered[36].

Ferrocene thiolate occurs as a bridging ligand in the gold complex *(10)*[51].



(10)

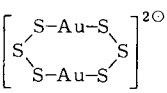
Gold atoms are also found as "ligands" of *chalcogenonium centers* in the complexes $[(LAu)_3S]^{\oplus}X^{\ominus}$, which are accessible with surprising ease *via* silyl sulfide precursors[52]. Triauriose-lenonium salts were obtained in similar manner[37]:

$$3\,R_3PAuCl + (CH_3)_3SiSeSi(CH_3)_3 \longrightarrow 2\,(CH_3)_3SiCl + [(R_3PAu)_3Se]^{\oplus}Cl^{\ominus}$$

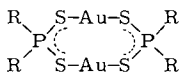
Unlike the silylthio derivatives, siloxy derivatives of Au^I do not suffer heterolysis to give oxonium salts[53]: compounds such as $R_3P{-}Au{-}OSi(CH_3)_3$, $R = CH_3, C_6H_5$, *etc.* are stable. However, *Nesmeyanov et al.* have described examples of triauriooxonium salts $[(R_3PAu)_3O]^{\oplus}X^{\ominus}$[54].

Bridged complexes having bidentate sulfur or selenium ligands

Monovalent gold has a pronounced tendency to form sulfur complexes, in which two metal atoms of coordination number 2 (and with linear configuration of their ligands) are components of an eight-membered ring. The oldest example, whose structure originally defied explanation[55], is probably the gold(I) trisulfide anion $AuS_3^{\ominus}$ shown by recent findings to require formulation as $Au_2S_6^{2\ominus}$:



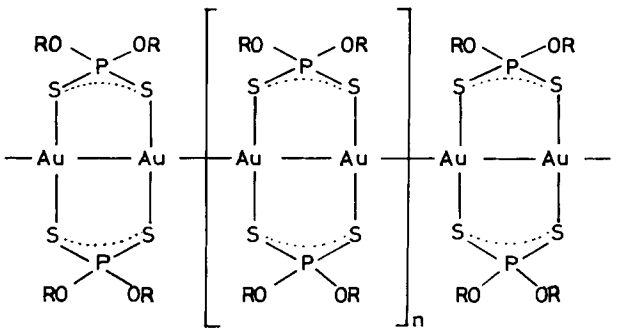
This compound was soon joined by Au^I *dithio-phosphates* and *-phosphinates* whose dimeric nature has been confirmed; X-ray data are also available[56].



(11), R = O-*i*-C_3H_7
(12), R = C_2H_5, C_3H_7, C_4H_9

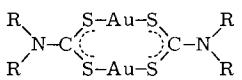
The dithiophosphates are suitable as additives to lubricants, being soluble in mineral oils and displaying novel lubricating phenomena by deposition of very fine noble metal coatings on mechanical and thermal stress. Crystal structure determination shows the diisopropyldithiophosphate *(11)* to be a

polymer containing a chain of gold atoms; like the dithiophosphinates *(12)* it exists as the dimer in solution[57].



Owing to their ready solubility and volatility, the dithiophosphinates *(12)* have been proposed for gas chromatographic isolation and detection of gold[58].

A second class of such sulfur complexes is found in the Au^I *dithio(or diseleno)-carbamates*. An example has also been subjected to X-ray analysis[59], and others to detailed analytical and spectroscopic studies[60–62].



The therapeutic potential of the thiophosphate and carbamate complexes has also been proposed for examination, but no final results have yet been published[2].

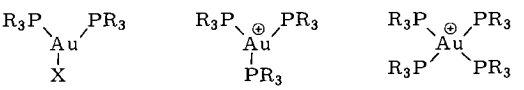
3.3. Phosphorus Compounds

In accord with present-day ideas of bonding in metal complexes, Au^I as a slightly charged, large, and easily polarizable metal ion forms particularly stable coordination compounds with phosphorus (and with sulfur). Very many complexes of this type are known, mainly with triorganophosphane ligands. Apart from the commonest types of compound

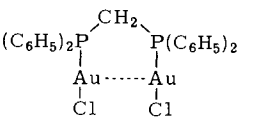
$R_3P–Au–X$

$[R_3P–Au–PR_3]^{\oplus}X^{\ominus}$

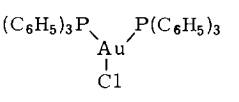
representatives having higher coordination numbers also exist[31]:



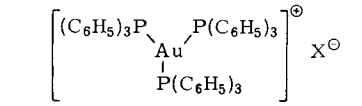
In the case of the simplest type R_3PAuX numerous new examples have been discovered in recent years[31,63–69]. The range of compounds extends from the complexes of phosphane itself (R = H)[70] *via* those of trialkyl-, triaryl-, and alkylarylphosphanes, to those of phosphites (R = OR') or aminophosphanes ($R = NR'_2$). These are supplemented by analogous arsane and stibane compounds. Halide, pseudohalide, carboxylate[71,72], and also carbaborane anions (*e.g.* 2,3-$B_4C_6H_7^{\ominus}$ and $B_{10}C_2H_{10}R^{\ominus}$, R = H, CH_3, C_6H_5)[73] may serve as ligand X[73]. The crystal structure of the 2:1 complex of AuCl with methylenebis(diphenylphosphane) has been elucidated[74a]. It shows a remarkably short Au—Au distance.



In compounds having *two* phosphane ligands, $(R_3P)_2AuX$, the structure is frequently dependent upon the environment. If X is a good leaving group then an ionic structure $[R_3P–Au–PR_3]X$ will be observed in the crystal, and certainly in solvating solvents[31,75]. In contrast, bis(triphenylphosphane)gold chloride *(13)* is not ionic in the crystal and contains Au^I having a coordination number of 3[76].



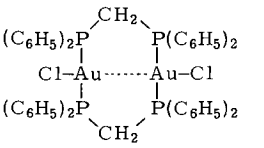
(13)



(14), X = B_9SH_{12}
(15), X = $Ta(CO)_6$

Trigonal-planar Au^I is also found in tris(triphenylphosphane)gold thiadecaborate *(14)*[77] and in the hexacarbonyltantalate *(15)*[78] whose structure has been confirmed by X-ray analysis. With less bulky phosphanes and large poorly coordinating ligands X even the $AuP_4^{\oplus}$ configuration may be achieved[31,78–80].

The 1:1 complex of AuCl and methylenebis(diphenylphosphane) has the structure of an eight-membered ring with weak transannular Au—Au interactions between trigonal planar metal atoms[74b]:



Triethylphosphanegold(I) chloride has recently been proposed for a hitherto unknown variant of gold therapy[81a]. It appears to display a number of important advantages over the sulfur compounds (thiomalate, thiogluconate, *etc.*) formerly used almost exclusively[81b]. The substance has a strong inhibitory action on mycoplasmic infections *in vitro*[82].

4. Gold(II) Compounds

4.1. Au^I/Au^{III} Compounds

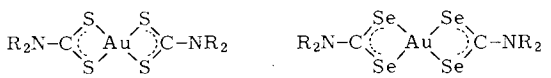
Compounds have long appeared in the literature in which gold formally has the oxidation number +2[83]. Meanwhile, it has been found that most of them are actually Au^I/Au^{III} combinations. Some representatives have been characterized by X-ray methods, and others by magnetochemistry or spectroscopy. In some cases simple analogies were sufficient:

Empirical formula	Structure
$AuSO_4$	$Au^IAu^{III}(SO_4)_2$
AuO, AuS	$Au^IAu^{III}O_2$, $Au^IAu^{III}S_2$
$Cs[AuX_3]$	$Cs_2[AuX_2][AuX_4]$; X = Cl, Br, I
$(C_6H_5CH_2)_2S \cdot AuX_2$	$(C_6H_5CH_2)_2SAuX$, $(C_6H_5CH_2)_2SAuX_3$
Au(Hdmg)Cl	$Au^IAu^{III}(Hdmg)_2Cl_2$
$(n\text{-}C_4H_9)_2NCS_2AuCl$	$[\{(n\text{-}C_4H_9)_2NCS_2\}_2Au]^{\oplus}AuCl_2^{\ominus}$

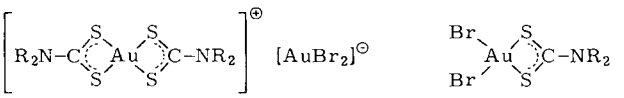
The presence of $Au_2^{4\oplus}$ in place of Au^I/Au^{III} has not been ruled out in the first two examples.

4.2. True Au^{II} Compounds

Recent studies have shown there to be four types of compounds qualifying as true gold(II) derivatives in which all the metal atoms have the same chemical environment. In addition to phthalocyanine-Au^{II}[84] ("AuPc") and an unusual carbaborane complex ("Au^{II} carbollide")[85], this class includes the *dithiocarbamates* of composition $Au(S_2CNR_2)_2$[86] first described in 1959. The uneven number of electrons (d^9 configuration of metal!) in these compounds, which are obtained by conproportionation of Au^I/Au^{III} or by reduction and oxidation, respectively, of Au^{III} and Au^I, has been detected primarily by ESR measurements. A bischelate structure is assumed, which probably also applies to the selenium analog[87].

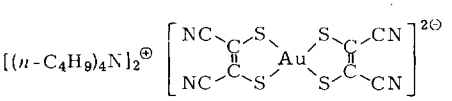


It should be pointed out that halodithiocarbamates such as *(16)* possess an Au^I/Au^{III} structure (cf. Section 4.1). The dihalodithiocarbamates have analogous configurations, *e.g.* *(17)*[28,88,89].



(16) *(17)*

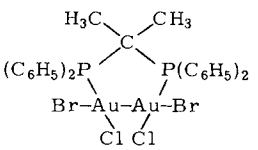
The fourth type of Au^{II} compound was discovered in the *cis*-1,2-dicyanoethylenedithiolates (*"maleonitriledithiolates"*), and is likewise accessible by a variety of synthetic approaches[90].



Identification was again accomplished by magnetochemistry and ESR spectroscopy [$\mu_{eff} = 1.85\ \mu_B$; $g = 2.009$, hyperfine splitting $A = 41.7$ G (^{197}Au: $I = 3/2$)]. Any remaining doubts as to the existence of true Au^{II} complexes were finally dispelled once the nature of these compounds had been established.

4.3. $Au_2^{4\oplus}$ Compounds

The AuCl complexes of methylenebis(phosphanes) undergo oxidative addition of one mole of halogen to yield formally a gold complex of oxidation state +II. Mössbauer and ESCA investigations have confirmed this proposal and the following formula is therefore assigned[91]:

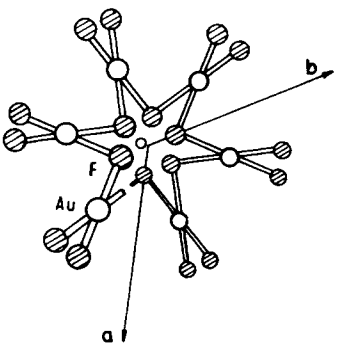


These products are diamagnetic, as expected, but a crystal structure determination has not yet been carried out. A new type of $Au_2^{4\oplus}$ compound is described in connection with organogold compounds (Section 7.5).

5. Gold(III) Compounds

5.1. Gold Trihalides and Their Halo Complexes

Gold forms trihalides only with fluorine, chlorine, and bromine. The structure of the trifluoride was long unknown. It was only the advent of modern improved methods of synthesis and single crystal growth, for which it is no longer a problem even with such a hard to handle substance as AuF_3, which permitted complete elucidation of its structure[92]. In contrast to the structure of the dimers of $AuCl_3$ and $AuBr_3$, this compound exists as helical polymers whose AuF_3 units are linked together *via* fluorine bridges:



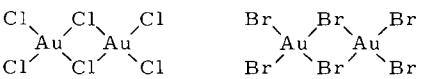
Gold trichloride, on the other hand, is dimeric in the solid state, in many solvents, and in the gaseous phase; it numbers among the most thoroughly studied compounds of gold[1]. A particularly convenient preparation was recently discovered[30]:

$$2\ H_3O^{\oplus}AuCl_4^{\ominus} + 2\ SOCl_2 \longrightarrow 2\ SO_2 + 6\ HCl + Au_2Cl_6$$

Furthermore, the first synthesis of a well-defined oxide halide AuOCl[93] has also been accomplished, and the enthalpy of formation of the oxide Au_2O_3 could be accurately determined[94]. Both compounds are hydrolysis products of the trihalides.

Gold(III) sulfide, selenide, and telluride halides are discrete phases in the gold/chalcogen/halogen system. Typical examples are AuSeCl, AuSeBr[95a,b], $AuTe_2Cl$, and $AuTe_2I$[95c]. In the gaseous phase, $AuCl_3$ and $FeCl_3$ form a complex $AuFeCl_6$[96].

The structure of gold tribromide, likewise a well-known compound, was determined only recently[97]; it closely resembles that of the trichloride.



Crystallographic data were also reported for $Rb[AuBr_4]$ and $Rb_2[Au_2Br_6]$[98].

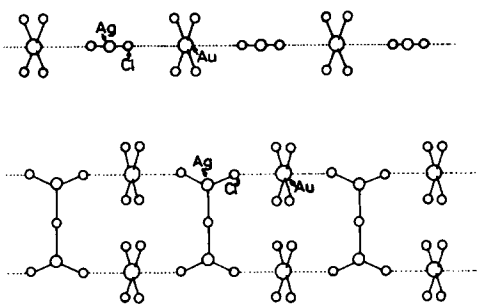
Such *haloaurate complexes*, and especially the tetrachloroaurate unit, are components of numerous salt-like compounds. Their structure and bonding are known[99-104]. $AuCl_4^{\ominus}$ will occur not only in crystalline compounds but also in molten salts[29].

Syntheses and structural elucidations of tetrafluoroaurates are almost all comparatively recent. The square-planar anion structure was confirmed for a series of alkali and alkaline earth salts. The potassium compound crystallizes in the $KBrF_4$ type[105].

$M^I[AuF_4]$ $\quad$ $M^{II}[AuF_4]_2$

M^I = Li, Na, K, Rb $\quad$ M^{II} = Mg, Ba

Among the mixed noble metal haloaurates, the particularly attractive structures of the complexes $Cs_2AuAgCl_6$ and $(NH_4)_6Au_3Ag_2Cl_{17}$ deserve special mention[106]:



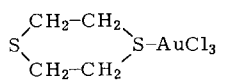
They are characterized by alternation of $AuCl_4^{\ominus}$ with $AgCl_2^{\ominus}$ and $Ag_2Cl_5^{3\ominus}$ groups [cf. also $Cs_2(AuCl_2)(AuCl_4)$ in Section 4.1].

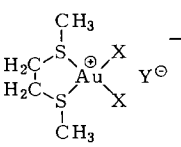
The mechanisms of reactions of the square-planar $AuCl_4^{\ominus}$ ion with various substrates have seen several attempts at elucidation; however, the individual reaction sequences often differ considerably[107-111] and thus defy generalization. Gold(III) pseudohalides have already been surveyed[33, 112, 113].

5.2. Compounds of Au^{III} with Sulfur, Phosphorus, and Other Elements

Gold(III) halides also form complexes with thioethers, but they are less stable than the gold(I) compounds. Fitting examples are[46, 47, 114]:

$(C_6H_5CH_2)_2S{-}AuCl_3$





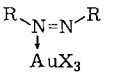
X	Y
Cl	$AuCl_4$
Cl	$AuCl_4 \cdot 2\ C_2H_5OH$
Br	Br
I	I

Corresponding coordination compounds exist with diphenylthiourea[115] and dimethyl sulfoxide[116], which is presumably coordinated *via* the S atom. The thiocarbamates[117], dithiomalonamides[118], and dithiooxamides[119] have already been mentioned in part[89].

Gold(III) *fluorosulfate* $Au(SO_3F)_3$, which does not strictly number among the gold-sulfur compounds, was synthesized just a few years ago; its structure has not yet been completely established[120].

As for other noble metals, an anhydrous *nitrato complex* of composition $[Au(NO_3)_4]^{\ominus}$ has also been obtained for gold[121]. The analytical data indicate the nitrato group to act as a unidentate ligand.

As expected, gold trihalides from stable complexes with nitriles[122], amines[123], phosphane oxides and sulfides[38, 124], and with triorganophosphanes. Trichloro(triphenylphosphane)gold has been studied by X-rays and shows the expected square-planar ligand arrangement[125]. In contrast to Au^I halides, those of Au^{III} also form complexes with azo compounds, which have an asymmetric structure[126]:



Older literature records the formation of "fulminating gold" on ammonolysis of tetrachloroauric acid. This complex reaction is currently being reinvestigated, and the stability constants of the Au^{III}-ammine complexes have been determined[127a] and the crystal structure of $[Au(NH_3)_4](NO_3)_3$ solved[127b]. The Au^{III} complexes of amino acids[128a, b], aldimines[128c], and tetracyclines[128d] cannot be discussed in the present report.

6. Gold(V) Compounds

Until a few years ago gold in the oxidation state +5 was unknown. Only in connection with the chemistry of noble gas halides did it become possible to accomplish the surprising synthesis of hexafluoroaurates(V); careful study left no doubt as to this new d^6 valence state of gold. Meanwhile, their synthesis is possible without the noble gas fluorides since other fluorination methods also lead to the desired result[129]:

$$AuF_3 + 2\ XeF_2 + 5\ F_2 \longrightarrow [F_5XeFXeF_5][AuF_6]$$

$$CsAuF_4 + F_2 \longrightarrow Cs[AuF_6]$$

$$AuF_3 + O_2 + 3/2\ F_2 \longrightarrow O_2^{\oplus}[AuF_6]^{\ominus}$$

The $AuF_6^{\ominus}$ ion is octahedral and corresponds to $PtF_6^{2\ominus}$ and other long-known analogous anions. Very recent work has extended the series of its salts to include $KrF[AuF_6]$[130]. Uncomplexed gold pentafluoride AuF_5 is formed as an orange powder on vacuum pyrolysis of the $KrF^{\oplus}$- or $O_2^{\oplus}$-hexafluoroaurates[130].

7. Organogold Compounds

7.1. Alkylgold(I) Complexes and Dialkylaurates(I)

Pure, not complex-stabilized alkylgold compounds RAu have not yet been isolated. However, the number of complexes derived therefrom is steadily increasing. A tabular summary of such triphenylphosphane complexes should underline the broad scope of the investigations performed so far[31, 131-136].

R—Au—PR'_3	R	R'	Ref.
	CH_3	CH_3, C_6H_5	[131a]
	C_2H_5, *n*-C_3H_7	C_6H_5	[134a]
	i-C_3H_7, *n*-C_4H_9	C_6H_5	[134a]
	s-C_4H_9, *t*-C_4H_9	C_6H_5	[134a]
	$(CH_3)_3CCH_2$	C_6H_5	[133, 134a]
	$(CH_3)_3SiCH_2$	C_6H_5	[132, 133]
	CH_3COCH_2	C_6H_5	[136a]
	CF_3	C_6H_5	[136b]

In addition to these examples the cyclopentadienyl compounds, which have been shown to possess a fluxional structure with an Au—C σ bond[137], also warrant mention. The ferrocene derivatives, in which the cyclopentadienyl group is also a constituent of the π-complex, represent an interesting variant of this compound type[138].

Nearly all the publications cited contain detailed information about the spectroscopic properties of the RAuL complexes[139]. The simplicity of their NMR spectra proved to be particularly useful in the study of their reactions[131,132,134,135].

It was already known that R—Au—L complexes react with alkylmetal compounds presumably forming $R—Au—R^{\ominus}$ anions[140]; however, these species could not be directly detected. Recent studies have now demonstrated that such products are stable both in the presence of stabilizing phosphane donors[141] and in solvate-free complexes[142] up to room temperature and even beyond. An example of the first-named case is:

$$CH_3AuP(C_6H_5)_3 + CH_3Li \longrightarrow (CH_3)_2AuP(C_6H_5)_3Li$$

The structure of the product is not accurately known[141]. If effective coordinative saturation of the lithium ion is ensured then the thermal stability increases sharply and salts are formed which are made up of linear dialkylgold anions and chelate cations, *e.g.*[142]:

$$[\{(CH_3)_2NCH_2CH_2N(CH_3)_2\}Li]^{\oplus}\,[CH_3-Au-CH_3]^{\ominus}$$

The compounds obtained in this way react with alkyl halides to form trialkylgold(III) complexes which decompose with reductive elimination of alkane under suitable conditions[141b,143]. They are therefore suspected to play a role in the formation of C—C linkages catalyzed by gold(I) salts, which start from alkylmetal compounds and alkyl halides[143]. Copper(I) salts are used more frequently for this reaction. The $R—Au—R^{\ominus}$ ions correspond to the neutral mercury compounds R—Hg—R.

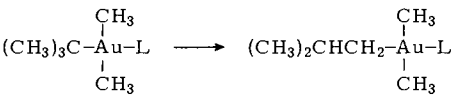
7.2. Oxidative Addition of Alkylgold(I) Complexes and Mechanistic Aspects

Methyl iodide reacts with methyl(trimethylphosphane)-gold(I), giving ethane and iodo(trimethylphosphane)gold(I) *via* unknown intermediates[144]. The initial step was interpreted as an oxidative addition to give an unisolable product. Subsequent investigations with other ligands then showed the reaction to take the following course[134b]:

$$CH_3Au\cdot L + CH_3I \longrightarrow (CH_3)_2AuI\cdot L$$
$$(CH_3)_2AuI\cdot L + CH_3Au\cdot L \longrightarrow (CH_3)_3Au\cdot L + L\cdot AuI$$
$$(CH_3)_3Au\cdot L \longrightarrow C_2H_6 + CH_3Au\cdot L$$
$$\overline{CH_3Au\cdot L + CH_3I \longrightarrow C_2H_6 + L\cdot AuI}$$

Thus CH_3AuL unexpectedly has a *methylating* action on the dimethylgold(III) iodide complex, giving the $(CH_3)_3Au$ complex which then decomposes with elimination of ethane. This final step is still unexplained, since pure $(CH_3)_3AuL$ is stable under the reaction conditions, and the by-products apparently catalyze its reductive decomposition[145].

Analogous reactions involving more complex alkyl groups attached to the gold atom can also lead to isomerization, mainly in the Au^{III} state[143]; one such process is the rearrangement of a *tert*-butyl group into an isobutyl group according to [143]:



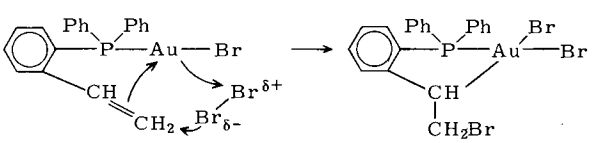
The rate of this rearrangement corresponds to a first-order reaction with respect to the concentration of complex, but is independent of the phosphane concentration [L]. Hence a predissociation to free L and trialkylgold is deduced. NMR measurements also suggested an associative mechanism to be unlikely for ligand substitution of R_3AuL complexes[131]; preparative experiments nevertheless demonstrated the ready substitution of L in the presence of an excess of competing ligands[131].

Alkylgold(I) complexes, but not alkylgold(III) complexes, surprisingly react with thiophenol by a radical mechanism[39,146].

7.3. Alkylgold(III) Complexes and Tetraalkylaurates(III)

Like free alkylgold(I) molecules, those of trialkylgold(III) are unknown. The number of complexes has rapidly increased, however, and many examples have been examined in detail. In addition to the $R_3Au\cdot L$ type itself[131,134,135], the monofunctional derivatives $R_2XAu\cdot L$ are particularly interesting; they generally exist as the *cis* isomers[147]. Most of these new compounds were obtained by conventional synthetic methods or as products of oxidative addition to alkylgold(I) complexes (cf. Section 7.2)[141–145].

A special case is seen in the formation of heterocycles by halogenation of an olefinic precursor and alcoholysis of the intermediate with ring expansion; this reaction is almost without precedent. The structure of these compounds has been established by X-ray methods[148].



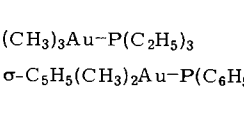
Tetraalkylaurates(III) have been synthesized in similar manner to the defined dialkylaurates(I). Coordinative saturation of the cation (Li^+) by polydentate ligands enhances the stability of the salts to such an extent that they can be isolated in pure form and can also be stored above room temperature[142]. The following formulas give some indication of typical alkylgold(III) compounds[132,149–151]:

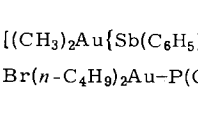
$(CH_3)_3Au—P(C_2H_5)_3$

$[(CH_3)_2Au\{Sb(C_6H_5)_3\}_2]^{\oplus}ClO_4^{\ominus}$

$\sigma\text{-}C_5H_5(CH_3)_2Au—P(C_6H_5)_3$

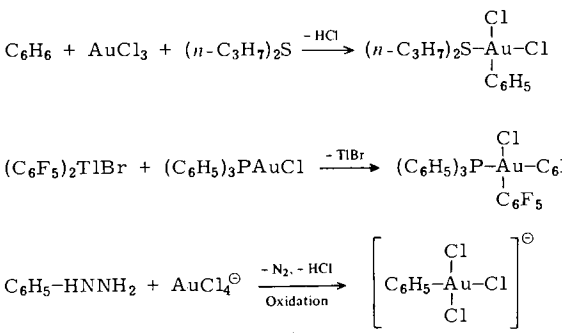
$Br(n\text{-}C_4H_9)_2Au—P(C_6H_5)_3$



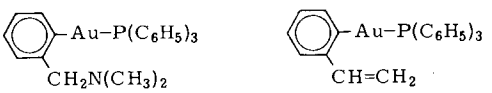


7.4. Arylgold(I) and -gold(III) Compounds

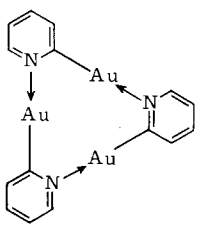
Arylgold compounds were practically unknown until very recently[3]; the first well-characterized examples date from 1972[152]. Meanwhile, considerable advances have been made in their preparation by improvement of the phenylation process[153-155], in particular by the use of phenylthallium reagents[156,157]. This applies above all to perhaloaryl derivatives. A selection of equations shows the synthetic methods used and the structures of the products, which have been confirmed in part by X-ray methods[158,159].



The first case is an example of the classical "auration" of aromatic compounds according to *Kharasch* and *Isbell*[160], which frequently gives poor results in other cases. Phenylgold(I) complexes such as $C_6H_5AuP(C_6H_5)_3$[155] were described by *Perevalova et al.*[155]. Their *ortho/para* substituted homologs display a pronounced thermal stability[161,162], *e.g.*



The structure of aurated pyridine[163], like that of 1-pyrazolylgold(I)[164] which is also trimeric, is a particularly attractive example of the wide range of structural variation.



7.5. Gold(I,II,III) Ylide Complexes

The considerable number of compound types and their manifold structural phenomena justify devotion of a separate section to the gold derivatives of phosphorus, arsenic, and sulfur ylides[165]. The compounds are distinguished by exceptional thermal stability and strongly modified chemical reactivity.

$CH_3-Au-CH_2-P(CH_3)_3$

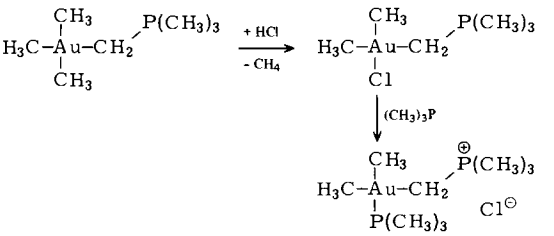
$(CH_3)_3Si-CH_2-Au-CH_2-P(CH_3)_3$

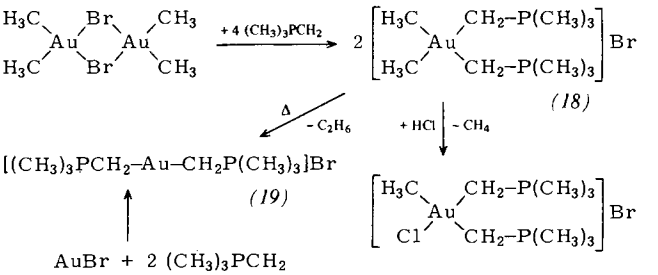
$[(CH_3)_3P-Au-CH_2-P(CH_3)_3]Cl$

$[(CH_3)_3P-CH_2-Au-CH_2-P(CH_3)_3]Cl$

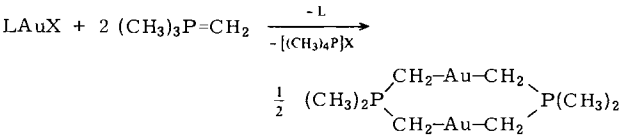
The prototype of this class is methyl(trimethylphosphoniomethylide)gold(I) and its homologs and the corresponding phosphane compounds and bis(ylide)gold salts[166a].

These substances arise from suitable gold(I) precursors by substitution of phosphane or halogen. Gold(III) ylide complexes are obtained analogously from trialkylgold components[166b]:

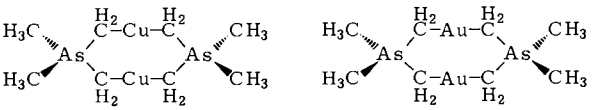




The bis(ylide)gold(III) salt *(18)* can be transformed into the bis(ylide)gold(I) salt *(19)* by thermally induced reductive elimination of ethane[166b]. A further type of gold-ylide complex is accessible by transylidation in the presence of an excess of ylide base. There result cyclic compounds in which two gold atoms have a linear arrangement of ligands[166c]:

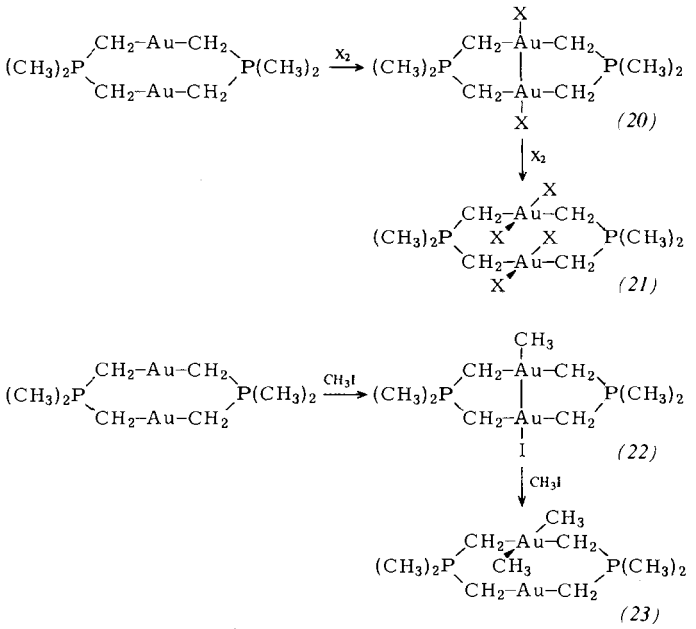


Such heterocycles have been prepared with various substituents on the phosphorus atom, and an arsenic analog has also been synthesized with $(CH_3)_3As{=}CH_2$[167]. The crystal structure of the corresponding copper compound is already known[168]. Recently, the structure of the ethyl-substituted gold analog was also determined[167].



On reaction with halogens, the above heterocycles initially afford bicyclic derivatives *(20)* having a transannular Au—Au bond[166c]. A crystal structure analysis is available for the ethyl compound[169]. Once again $Au_2^{4\oplus}$ units, and thus gold atoms in the formal oxidation state +2 (cf. Section 4.3), are encountered. On treatment with methyl iodide, oxidative addition proceeds as with halogen to give a product *(22)* which yields *(23)* on methylation[166c].

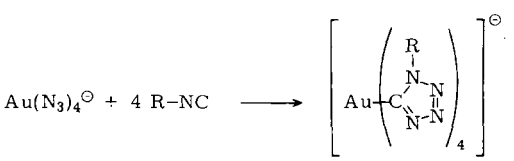
Further halogenation of the dihalides *(20)* finally results in rupture of the Au—Au bond to give the Au^{III} heterocycle

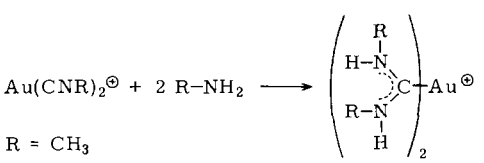


(21). Mössbauer and ESCA spectra confirm the different valence states of the metal atoms in the products *(20)* and *(23)*[170].

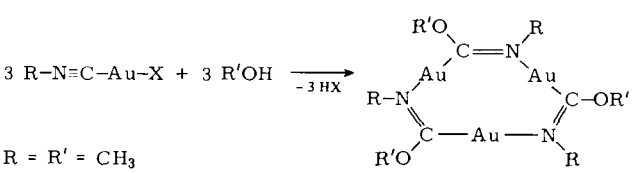
7.6. Carbene Complexes of Gold

In the course of the rapidly developing chemistry of metal-carbene complexes, Au^{I} and Au^{III} have been examined to establish their suitability as coordination centers for carbenoid ligands. Thus was born a new subdiscipline of organogold chemistry. The first examples of such compounds were obtained by addition reactions with isocyanides[171,172] or their complexes[173-175]:

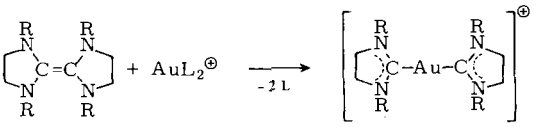




X-Ray structural data are available for all types[171b,176]. Monoisocyanide complexes form cyclic products with alcohols[177]:



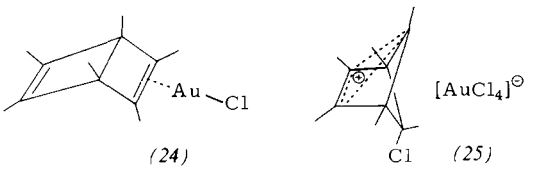
A new synthetic procedure for carbene complexes, as shown in the following equation, is applicable to many metals and gives very good yields in the case of Au^{I}[178]:



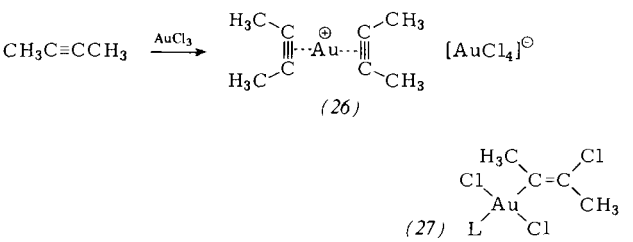
7.7. Reactions of Alkenes and Alkynes with Gold Compounds

Studies by *Hüttel et al.*[179] have shown that above all gold(I) salts can form π-complexes with a whole series of olefins, some of which display pronounced stability. These findings have mainly been surveyed on an earlier occasion[3].

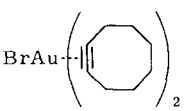
In more recent studies, interest has been focused on more specific problems, *e.g.* on the reaction between hexamethyl-Dewar benzene and gold trichloride, which leads to an AuCl complex *(24)* of the hydrocarbon and to the tetrachloroaurate of its monochlorination product *(25)*[179b].



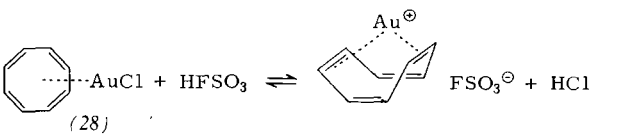
The interaction of acetylenes with gold halides leads in the case of dimethylacetylene[180] to π-complexes, *e.g. (26)*, which, however, rearrange into σ-compounds such as *(27)* under mild reaction conditions.



Cyclooctyne reacts with AuBr to give a 2:1 complex of unknown structure which possesses a remarkably high stability[181].



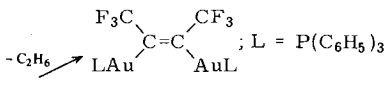
Cyclooctatetraene forms only a very weak complex *(28)* with AuCl; its formation constant was determined as $K = 9.1$ l/mol[182]. Its reaction with fluorosulfuric acid gives a presumably ionic product:



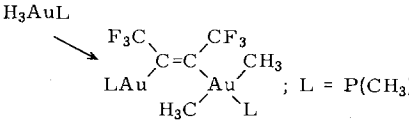
(28) and $AuCl_3$, as well as COT and $AuCl_3$ (with partial reduction to AuCl), give an unstable complex of composition $COT \cdot Au_2Cl_4$, whose Mössbauer spectrum clearly reveals the Au^{I}/Au^{III} combination; an unequivocal structure could not yet be assigned[182].

In the case of fluoroolefins practically no π-coordination occurs, either with Au^{I} or with Au^{III}—instead insertion or elimination is observed in all cases reported so far[183]:

$C_2F_4 + CH_3AuL \longrightarrow CH_3CF_2CF_2AuL$



$CF_3{-}C{\equiv}C{-}CF_3 + 2\ CH_3AuL$



In the last example, the structure of the reaction product was proved by X-ray analysis and by Mössbauer spectroscopy[184a] after other proposals had originally been put forward[184b].

With $CF_3C{\equiv}CH$, CH_3AuL and $(CH_3)_3AuL$ give the products $LAu{-}C{\equiv}C{-}CF_3$ and *cis*-$(CH_3)_2AuL{-}C{\equiv}C{-}CF_3$, respectively[184b].

The examples of olefin/gold interaction listed above suggest that this metal could also assume a role as a catalyst in olefin reactions. Indeed, strong supporting evidence is already available, for example in the electrooxidation of ethylene at gold electrodes[185]. Current-carrying gold surfaces also catalyze the air-oxidation of propene, the reaction displaying considerable selectivity[186]. Tetrachloroauric acid on a silica support catalyzes the hydrogenation of olefins[187]. Hydrogenation of ethylene is catalyzed by $HAuCl_4$ in the presence of SbX_5[188].

The recently synthesized gold(I) ketenide Au_2C_2O[189] also appears to show a catalytic activity[190] resembling that of gold(I) acetylide[191].

A final example of a pronounced catalytic activity of gold has been obtained very recently. A gold film condensed onto a support material catalyzes hydrogen/deuterium exchange of alkylsilanes at as low a temperature as 195 K[192]. Surprisingly, however, this effect disappears at room temperature!

In conclusion, reports should also be mentioned according to which microorganisms are capable of enzymatic dissolution of elemental gold, and could therefore be made responsible for leaching out gold-bearing rock and enriching the metal in concentrated deposits. This "bioorganic aspect" again shows the kind of surprises to be expected in gold chemistry.

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Hormone Receptors

By Klaus Lübke, Ekkehard Schillinger, and Michael Töpert[*]

Corpora non agunt nisi fixata — *Paul Ehrlich (1845—1915)*

Hormone receptors are proteins located on the cell membrane or in the cell cytoplasm. Their function is to recognize and bind the respective hormone; the biological action of the hormone originates from the hormone-receptor complex. Specific receptors have been found for all known hormones. Monitoring the equilibration between hormone, receptor, and hormone-receptor complex ("determination of receptor binding") permits quantitative determinations of hormones, allows the characterization of endocrinal disturbances, and contributes to the elucidation of structure-affinity relationships.

1. Introduction

A common feature of all hormones is their participation in the control of biological processes. Hormones function by transmitting information which leads to a triggering of cell-specific activities. They can only fulfil the role of a "first messenger" if recognized by their target organs and distinguished from other compounds. A decisive step in the recognition process is the binding of the hormone to its receptor (a protein). The biological activity of a hormone (or a hormone analog) is determined by the concentration of the hormone-receptor complex at the site of action and by the intrinsic activity[1, 2] of the complex. The concentration of the hormone-receptor complex depends upon the availability of the hormone at the site of action and upon its affinity for the receptor (Fig. 1).

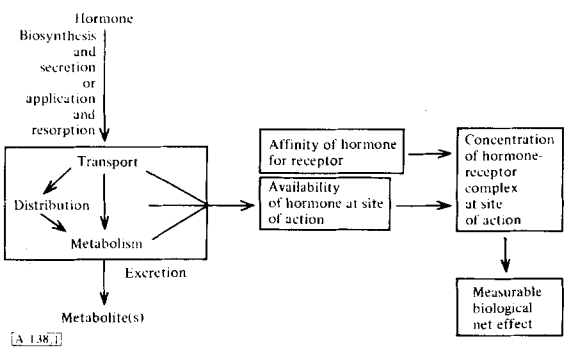

Fig. 1. Factors affecting the concentration of the hormone-receptor complex, and hence the biological activity, *in vivo*.

The hormone-receptor complex may be formed on or inside the cell. In the former case the hormone finds its specific receptor on the surface ot the cell membrane. There is no need for it to penetrate into the cell; instead it triggers an intracellular process by binding to the membrane-bound receptor. In the latter case the hormone does have to penetrate into the cell before a hormone-receptor complex can be formed. The former group includes all peptide and proteohormones, the biogenic amines, and the prostaglandins, while the latter group comprises all steroid hormones, thyroxine, and triiodothyronine.

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2. The Hormone-Receptor Complex

The existence of specific hormone receptors and their importance in hormone action were postulated long ago[3]. However, experimental detection of the receptors, present only in very low concentration, was long thwarted by the lack of suitable experimental methods, and only became possible once hormones could be labeled with sufficiently high specific radioactivity. In the early 1960's *Jensen et al.* used tritium-labeled estradiol to characterize the first cytoplasmic (intracellular) hormone receptor[4]. A few years later *Cuatrecasas*[5], *Lefkowitz et al.*[6], and *Goodfriend et al.*[7] were able to detect the first membrane-bound receptors using ACTH, insulin, and angiotensin, respectively, labeled with radioactive iodine. Specific receptors were subsequently reported for all hormones and concepts formulated for hormone-receptor binding and its significance for hormonal action.

2.1. Definition of the Hormone Receptor

A hormone receptor has to fulfil a number of requirements[8]:

1) The specificity of the receptor must be very high and comply with known structure-activity relations.

2) The number of binding sites must be limited.

3) The occurrence of receptors in various tissues should correlate with the response of the respective tissue to the hormone.

4) Owing to the very low physiological concentrations of hormones the receptor must have a high affinity for the hormone.

5) Hormone-receptor binding must be reversible in order to terminate the physiological effect and permit fresh stimulation.

It is important to distinguish between receptor binding, characterized by high affinity with low capacity, and non-specific binding to other hormone-binding proteins. The latter typically exhibits a low affinity at very high capacity.

2.2. Membrane-Bound Hormone Receptors

The intracellular sequence of reactions triggered by binding of a hormone to its membrane-bound receptor is determined not by the hormone but rather by the properties of the cell. Thus adrenocorticotropic hormone (ACTH) and interstitial cell stimulating hormone (ICSH, LH) stimulate the same reaction, *viz.* conversion of cholesterol into pregnenolone (3-hydroxy-5-pregnen-20-one). The fact that different end products are formed (mainly corticoids in the adrenal cortex and mainly androgens, estrogens, and gestagens in the germ cells) is attributable to the specific enzymatic pattern of these cells (Fig. 2).

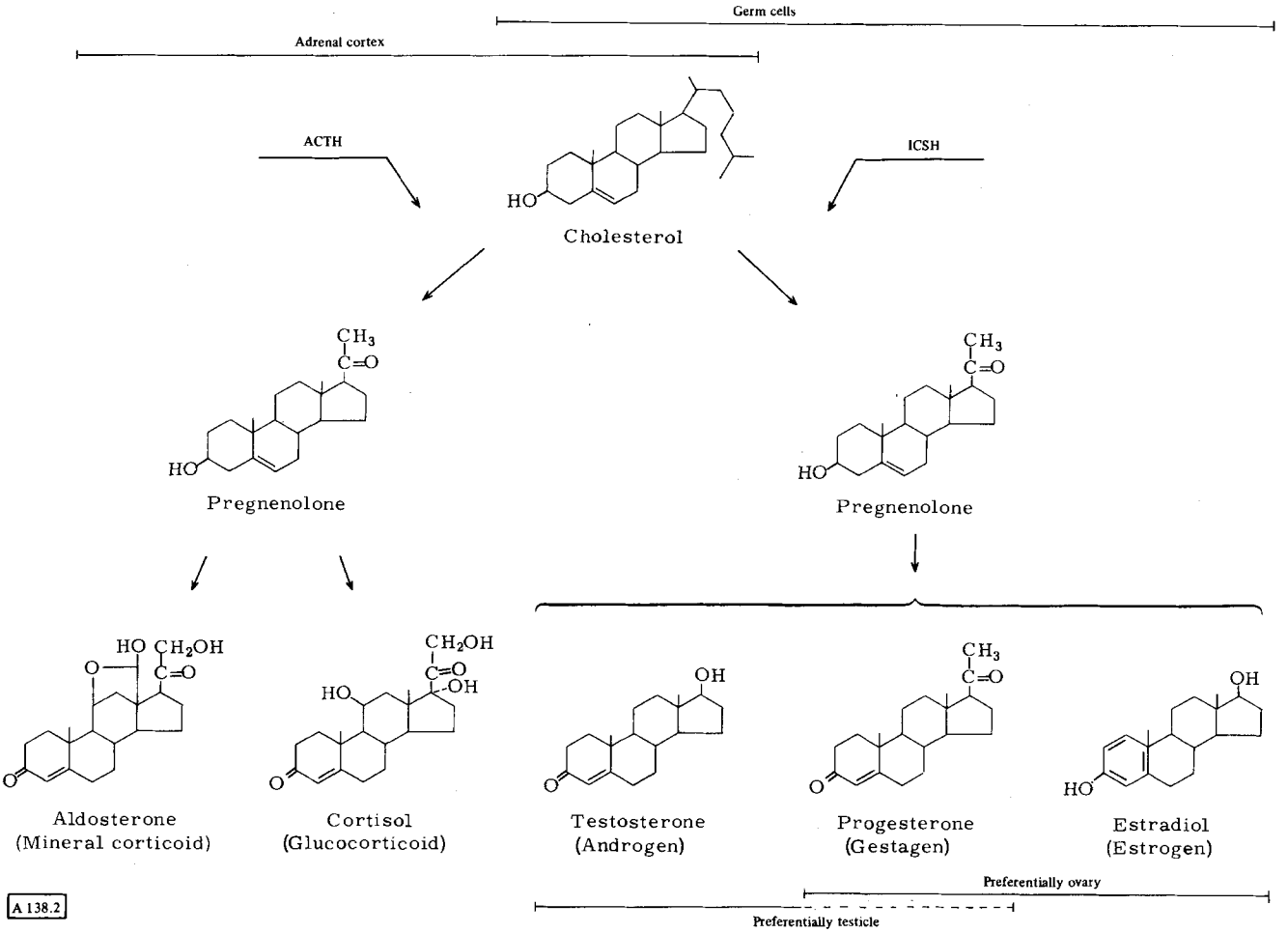

Fig. 2. Hormonal stimulation of steroid production in the adrenal cortex and in the germ cells (according to ref. [7a]). ACTH, adrenocorticotropic hormone; ICSH, interstitial cell stimulating hormone.

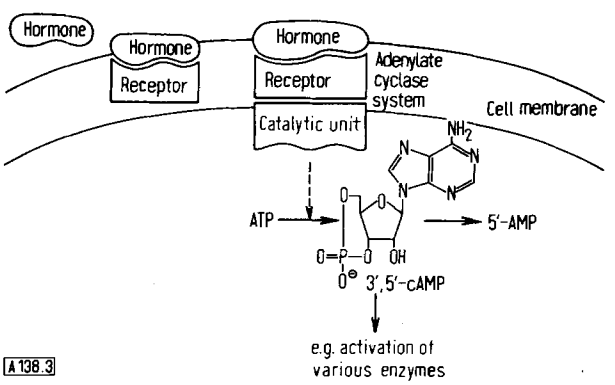

Fig. 3. Scheme of hormone action *via* a membrane bound receptor.

The intracellular processes are controlled by a "second messenger". In many cases this role is fulfilled by cyclic 3',5'-adenosine monophosphate (3',5'-cAMP) (Fig. 3). However, 3',5'-cAMP can only be produced from ATP once the enzyme adenylate cyclase has been activated. *Cuatrecasas*[8] has postulated that the receptor and the enzyme initially occur separately in the membrane. It is then the hormone-receptor complex which combines with the enzyme and effects its activation.

2.3. Cytoplasmic Hormone Receptors

Binding of the hormone to a cytoplasmic (intracellular) receptor requires that the hormone penetrates into the cell. Whereas a simple diffusion was formerly assumed to be responsible, evidence now exists that transport into the cell is a specific process, possibly controlled by membrane-bound proteins[9]. The hormone-receptor complex is first formed within the cell and, after activation, can penetrate into the cell nucleus (Fig. 4). This activation is temperature-dependent and linked with a change in the sedimentation constant[10]. Several models have been proposed to account for formation and activation of the complex, *e. g.* involving allosteric processes, dimerization of the hormone-receptor complex, and its aggregation with other proteins. An acceptor specific for the hormone-receptor complex is assumed to exist in the cell nucleus, which, for example, effects synthesis of the proteins important for hormonal action *via* transcription and translation by switching off a repressor.

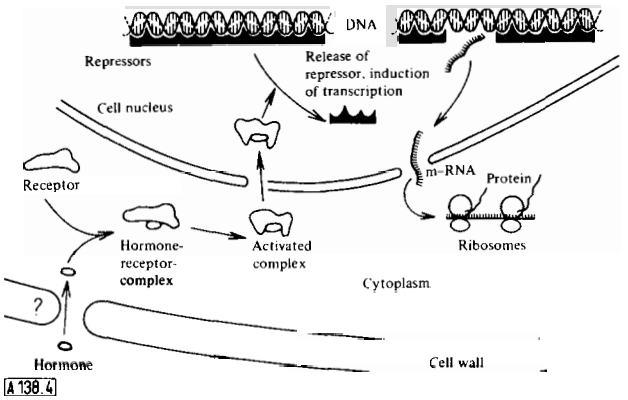

Fig. 4. Scheme of hormone action *via* a cytoplasmic receptor

3. Formation of the Hormone-Receptor Complex

Studies on the formation of the hormone-receptor complex should take into account the following theoretical and practical problems.

3.1. Formation of the Hormone-Receptor Complex as an Equilibrium Reaction

To understand hormone(H)-receptor(R) binding it is sufficient to consider the following two equilibria for membrane-bound receptors (a) and cytoplasmic (intracellular) receptors (b) respectively:

a) Membrane-bound receptor

$$H + R \rightleftharpoons H{-}R \xrightleftharpoons[\text{Cyclase}]{} H{-}R{-}\text{Cyclase}$$

b) Cytoplasmic receptor

$$H + R \rightleftharpoons H{-}R \rightleftharpoons H{-}R_{\text{activated}}$$

These are formation of the hormone-receptor complex H – R (for a and b) and activation of the cyclase system (cf. Fig. 3) for (a) and temperature-dependent activation of the hormone-receptor complex (cf. Fig. 4) in case (b). Depending on the kind of binding assay and on the experimental conditions, either the first equilibrium only or more or less the sum of the two equilibria will be determined.

3.2. "Direct" Determination of the Receptor Binding

If the hormone or hormone analog is present in radioactively labeled form then its binding to the receptor is open to direct measurement. The readily measurable concentrations of the hormone-receptor complex (H – R) and of the free hormone (H) are preferentially used as variables. Graphic representations of complex formation leading to straight lines are of considerable advantage (Fig. 5)[11]. Slope and intercepts permit calculation of binding parameters. Most frequent use is made of the equation reported by *Scatchard*[12] (cf. also Fig. 5e), which is derived as follows:

$$H + R \rightleftarrows H{-}R \text{ and } \frac{[H-R]}{[H][R]} = K$$

Putting

$$[R] = [R_0] - [H-R]$$

then

$$\frac{[H-R]}{[H]\cdot([R_0]-[H-R])} = K$$

or

$$\frac{[H-R]}{[H]} = K\cdot([R_0]-[H-R])$$

$$\frac{[H-R]}{[H][R_0]} = K\cdot\frac{[R_0]-[H-R]}{[R_0]}$$

$$\frac{[H-R]}{[H][R_0]} = K\cdot\left(1-\frac{[H-R]}{[R_0]}\right)$$

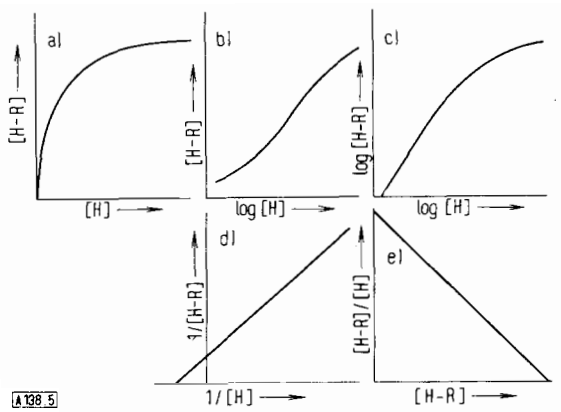

Fig. 5. Plot of formation of the hormone-receptor complex (H – R). a) [H – R] = f[H]; b) [H – R] = f(log[H]); c) log[H – R] = f(log[H]); d) 1/[H – R] = f(1/[H]); e) [H – R]/[H] = f([H – R]) (plot according to *Scatchard*).

In practice, the overall concentration of receptor $[R_0]$ is used instead of the generally unknown concentration of free receptor [R]; $[R_0]$ is assumed to be proportional to the readily measurable concentration of protein. The slope of the straight line gives the affinity constant K, and the intercept with the abscissa provides a measure for the number of binding sites.

Application of the law of mass action requires that the measurements be performed below the saturation range of the receptor (Fig. 6). After equilibration, the free and receptor bound hormone are separated and assayed. The receptor concentration in a preparation is normally of the order of $<10^{-8}$ mol/l. Determination of such low concentrations is only possible with hormones having specific activities of more than 10 Ci/mmol. Tritium and, in the case of proteohormones, iodine isotopes are used in practice. The presence of one or more tritium atoms in a molecule has hardly any effect on its affinity for a receptor. However, incorporation of an iodine atom, having roughly the same size as a benzene ring, may well modify the stereochemistry and physical chemistry of the molecule and thus impair its affinity towards the receptor. The situation is further complicated by the fact that

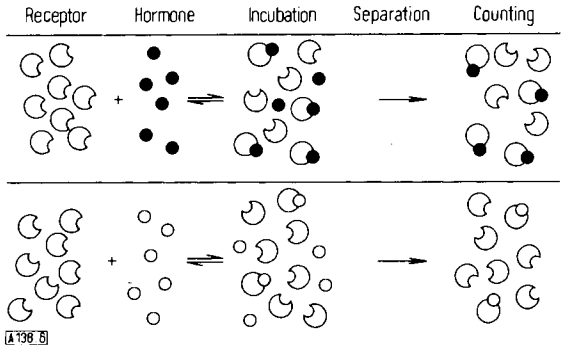

Fig. 6. Schematic representation of "direct" measurement of receptor binding. ●, hormone with high affinity; ○, hormone with slight affinity for the receptor.

more than one amino acid may be iodinated in most proteohormones. Hence the presence of several analogs displaying various degrees of iodination, and possibly different affinities for the receptor must be expected, together with non-iodinated hormone. The synthesis of analogs of insulin mono-iodinated at various sites demonstrated that these derivatives may cover the entire spectrum from inactive to fully active[13-15].

Graphical representations permit scrutenization of theoretical binding models by comparison of calculated and experimental plots. Thus a Scatchard plot in which an increase up to a maximum precedes the linearly decreasing range indicates a cooperative effect in complex formation (Fig. 7a).

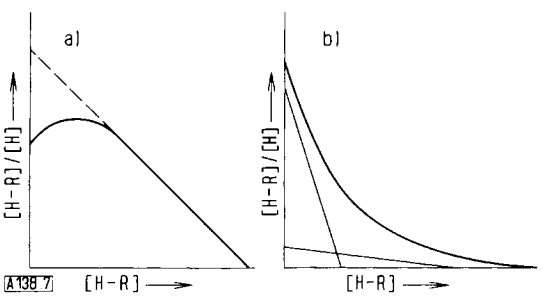

Fig. 7. Scatchard plot, a) for cooperative binding and b) in the presence of two binding sites.

The Scatchard equation occasionally results in a continuous curve. This can be attributed to the presence of more than one binding site. Such curves can be resolved graphically[16] or by computer iteration into two or more straight lines (Fig. 7b). In this way two binding sites have been demonstrated for many hormones such as insulin and prostaglandins[17, 18].

A non-linear Scatchard curve may also arise because a mixture of compounds having different affinities was present instead of a homogeneous hormone. This is to be expected primarily with iodinated proteohormones[19, 20].

In the "direct" measurement of receptor binding it must be assumed that not only formation of the hormone-receptor complex but also the second equilibrium—activation of the cyclase system or of the cytoplasmic receptor complex—are also monitored. The resulting apparent association constants are then too high.

3.3. Determination of Hormone-Receptor Binding by the Method of Competitive Protein Binding

The method of competitive protein binding must be used if the test substance (hormone or hormone analog) is not present in radioactively labeled form. This technique requires a radioactively labeled reference substance. The proportion of reference sample bound by the receptor is reduced by the test substance (Fig. 8). This reduction of receptor binding is termed competition. It depends upon the concentration

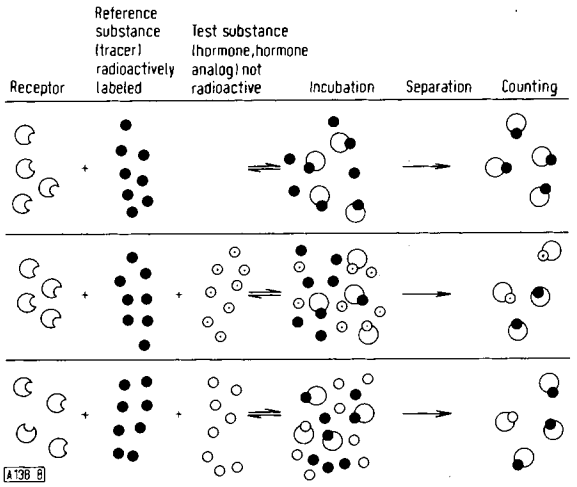

Fig. 8. Schematic representation of competitive determination of receptor binding. ●, radioactively labeled reference (tracer); ⊙, nonradioactive test substance (hormone) having the same affinity for the receptor as the reference substance; ○, nonradioactive test substance (hormone) having less affinity for the receptor than the reference substance.

of sample and upon its affinity towards the receptor. In contrast to the "direct" determination of binding, the measurements must be performed in the saturation range of the receptor. After incubation, the binding sites of the receptor are saturated; the subsequent reaction (activation of the cytoplasmic hormone-receptor complex or of the cyclase system) should therefore have no effect on the ratio in which reference substance and the sample are bound.

The competition curves obtained for varying concentrations of sample at constant concentration of reference substance have a sigmoidal shape typical for protein binding. They can be linearized within a wide range, for example by the logit-log transformation originally developed by *Rodbard* for radioimmunoassays[21] (Fig. 9).

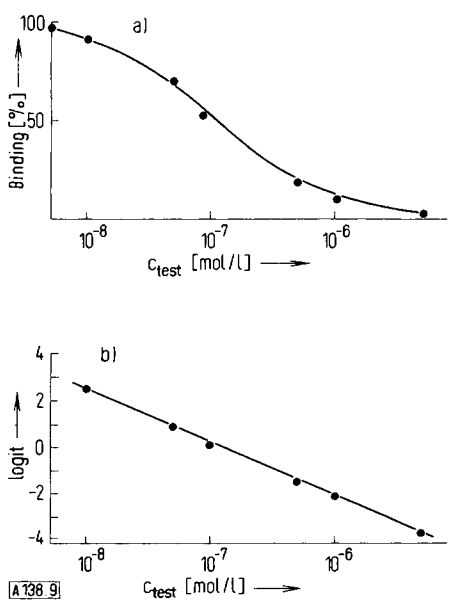

Fig. 9. a) Competition curve and b) its linearization by logit-log transformation according to *Rodbard* [21]. $\ln[\%\text{ binding}/(100-\%\text{ binding})] = f(\log c_{test})$. c_{test} = concentration of test substance.

A drawback of the method of competitive protein binding is that the competition curves obtained for several samples with the same receptor are often not parallel. The relative affinity therefore cannot be calculated simply from these competition curves. Considerable experimental and mathematical effort would be required. In practice, this problem is circumvented by relating arbitrarily selected points on these curves, usually that of 50 % competition, with one another. Experience gained with non-parallel competition curves can be confirmed by simulation on an analog computer and by calculation of such curves[22] (Fig. 10).

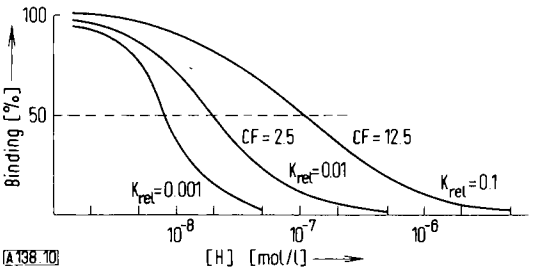

Fig. 10. Competition curves obtained by simulation on an analog computer. K_{rel} = relative association constant (given), CF = competition factor. See text for details.

The three curves which were calculated for relative dissociation constants (K_{rel}) of 0.1, 0.01, and 0.001 are not parallel. Moreover, the concentrations determined for 50 % competition are not in the ratio 1:10 and 1:100, but 1:2.5 and 1:12.5. These values should therefore not be designated as relative affinities. Instead the term "competition factor" (CF) has been proposed. It is defined as the ratio of the concentration of the test sample (c_{test}) and that of the reference substance ($c_{ref.}$) required for 50% competition:

$$CF = \frac{c_{test} \text{ at } 50\,\% \text{ competition}}{c_{ref.} \text{ at } 50\,\% \text{ competition}}$$

4. Receptor Preparations

Receptor preparations are preferentially obtained from typical target organs of the respective hormone. For some hormones several kinds of tissue are suitable (Table 1).

Table 1. Tissues suitable for receptor preparations.

Hormone	Tissue
ACTH (adrenocorticotropic hormone)	Adrenal cortex
Calcitonin	Kidney, bone, lymphocytes
Glucagon	Liver, pancreas, adipose tissue, heart
Gonadotropins:	
HCG (human choriongonadotropin)	Testes, ovary
LH, ICSH (interstitial cell stimulating hormone)	Testes, ovary
FSH (follicle stimulating hormone)	Ovary
Insulin	Liver, adipose tissue, lymphocytes, muscle
Catecholamines	Myocardium, liver, erythrocytes, uterus, adipose tissue, brain
Oxytocin	Frog skin, mamma, adipose tissue, uterus
Prolactin	Mamma
Prostaglandins	Uterus, ovary, adipose tissue, liver, kidney, adrenal cortex, thyroid, thrombocytes

The choise of tissue often depends upon the problem to be solved. Thus the relationship between insulin and lipid metabolism are best studied with receptors of fat cells or of the liver. The choice of animal species can also be important. For instance, considerable concentration differences could be established for corticoid receptors[23] in various species (Table 2).

Table 2. Concentration of corticoid receptor in rat and rabbit tissue.

Tissue	Juvenile rat	Juvenile rabbit
	[pmol receptor/mg protein]	
Liver	0.64	0.12
Skeletal muscle	0.06	0.03
Heart	0.26	0.13
Brain	0.19	0.12
Kidney	0.23	0.16
Testes	0.15	0.22
Thymus	0.45	0.65
Lung	0.02	0.53
Stomach	0.08	0.19
Spleen	0.07	0.27

Isolation of a receptor is extremely difficult. Therefore crude receptor preparations are frequently used. The procedure for cytoplasmic receptors is relatively simple. The cytosol available after homogenization of the tissue and centrifugation is employed almost exclusively as sample preparation.

The preparation of a membrane-bound receptor offers more variation. Reports have been published using intact discrete cells (*e.g.* erythrocytes, lymphocytes) or cells liberated from tissue by treatment with proteolytic enzymes (liver cells, fat cells, *etc.*). Use of intact cells often permits examination of subsequent biological reactions, *e.g.* activation of the adenylate cyclase system, parallel to hormone binding studies. Rather impure membrane fractions are often employed as receptor preparations instead of intact cells. Membrane-bound receptors have also been successfully solubilized by treatment with preferably nonionic detergents, without significantly affecting the binding. However, it has yet to be proved that such a soluble hormone-receptor complex still has a biologically relevant intrinsic activity after reconstitution.

5. Receptor-Binding Assay

The receptor preparation must be incubated with the hormone under conditions ensuring stability of the receptor and equilibrium (see Sections 3.1). Experiments with the rather unstable soluble (cytoplasmic) receptors are usually performed between 4 and 15 °C, rarely at higher temperatures. Incubation of the more stable membrane-bound receptors are often carried out at room temperature, and sometimes at 37 °C. Equilibrium is generally reached within a few minutes to several hours. Separation of free and receptor-bound hormone requires special attention; it should be performed under conditions where dissociation of the hormone-receptor complex is minimal. A compromise usually has to be met between optimal separation and time-saving performance.

Different separation techniques are described in the available literature. Density differences are exploited in separation by ultracentrifugation[23a]. For larger differences in density, *e.g.* for membrane fractions or intact whole cells, low speed centrifugation will suffice[40]. A particularly elegant

method for fat cells consists in floatation through an oil layer of intermediate specific gravity[23b]. Separation by molecular size can be accomplished with membrane filters[23c] or by gel chromatography[23d]. Charge differences are utilized in gel electrophoresis[23e]. Separation is also possible by binding the free hormone to adsorbents. These adsorption procedures, specifically with dextran-coated activated charcoal, find frequent application. They do have the drawback, however, that the pronounced affinity of the adsorbent for the hormone can interfere with the equilibrium. In all separations it is advisable to work at low temperature to suppress dissociation of the hormone-receptor complex.

6. Applications of the Receptor-Binding Assay

Having discussed the theoretical and methodological principles of the receptor-binding test, its applications will now be discussed (with the aid of selected examples).

6.1. Radioreceptor Assay as a Method of Quantitative Hormone Determination

Like a radioimmunological assay[22a], the radioreceptor assay can be used for determining hormone concentrations in tissue samples and body fluids. A hormone-specific receptor preparation is used instead of antibodies.

Whereas a radioimmunoassay will embrace structurally similar compounds, irrespective of their biological activity, a radioreceptor assay will register all substances having the hormone-specific biological activity, regardless of whether they are structurally related to the original hormone.

The generally low stability of the receptors compared with the immunoglobulins can be a handicap. This is particularly true for cytoplasmic receptors; the only assay so far reported with these receptors is one for estradiol[24]. Assays with the more stable membrane-bound receptors have been described for ACTH[25], glucagon[26], insulin[27], growth hormone[28], and the gonadotropins[29-31] and prostaglandin E_2[32]. Based on the receptor assay for HCG (human choriongonadotropin), an extremely sensitive pregnancy test has been developed which can already detect a pregnancy six to eight days after conception[33].

6.2. The Receptor-Binding Assay for Characterization of Endocrine Disturbances

In some cases it has been possible to correlate endocrine disorders with the receptor content of the relevant tissue. The relationship between disturbances of carbohydrate and lipid metabolism and the content of insulin receptors has been studied particularly thoroughly. In the carbohydrate and lipid metabolism of man and animals several pathological states are characterized by an increased or diminished insulin level in the plasma[34]. The concentration of insulin receptors measured in such cases appears to be inversely correlated with the insulin concentration (Table 3). Thus it was deduced that insulin itself regulates the receptor concentration. At high insulin levels the equilibrium will be shifted strongly in favor of receptor-complex formation. Therefore, a low number of receptor molecules will suffice for the full biological activity of insulin. Conversely, at low insulin concentrations

Table 3. Relationship between insulin concentration in the plasma and insulin receptor concentration (measured in various tissues) in endocrine disorders. ↑, increased; ↓ decreased concentration.

	Insulin concentration	Receptor concentration
Man:		
Obesity	↑	↓
Obesity + Diet	normal	normal
Maturity-onset diabetes	normal or ↑	↓
Maturity-onset diabetes + Sulfonylurea	normal	normal
Animal:		
Diabetes		
(Chinese hamster)	↓	↑
Hypophysectomy	↓	↑
Adrenalectomy	↓	↑
Corticoid excess	↑	↓

complex formation will be promoted by increasing the receptor concentration[35, 36]. It could be shown in animals and man that essentially normal receptor concentrations are re-established on reaching a normal insulin level after normalizing the pathological state, *e.g.* by a suitable diet.

Current interest is presently focused upon assays for estrogen receptors in cases of breast cancer (mammacarcinoma). Approximately one half of the tumor tissue samples could be shown to contain estrogen receptors (hormone-dependent tumors). Tumors which are not affected by treatment with estrogens are termed autonomous[37-39].

In the case of estrogen-dependent tumors a regression can often be achieved by treatment with antiestrogens, and less frequently with androgens. Hormone therapy is often supported by ovarectomy, adrenalectomy, and occasionally by hypophysectomy in order to stop production of endogenous hormones. A regression is observed in about 60% of the cases treated in this way. Hormone treatment and ablative surgical measures are generally unsuccessful in the case of autonomous tumors. Such tumors require administration of cytostatics (Fig. 11).

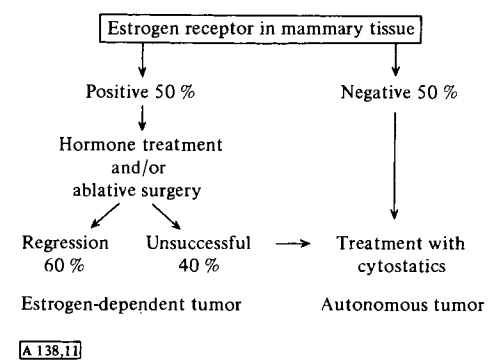

Fig. 11. Treatment of a mammacarcinoma depending upon its content of estrogen receptor.

The receptor-binding assay permits classification of the tumor and thus indicates the necessary form of treatment. In the case of autonomous tumors drastic surgery can then be avoided.

6.3. Receptor-Binding Assay to Determine Structure-Affinity Relations

The receptor-binding assay plays an important role in studies on structure-activity relations of hormones. The principal goal of such work, known generally as drug design, is the

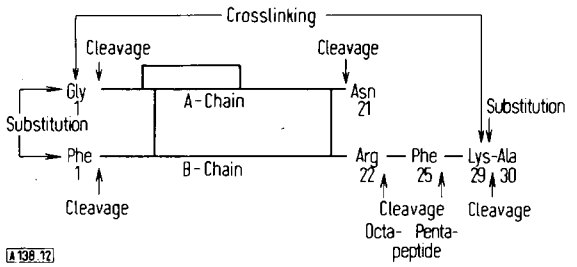

Fig. 12. Structural modification of insulin.

development of active compounds superior to the native hormone. Potentially interesting compounds are those having enhanced activity, which can be achieved by a higher concentration at the site of action, by a higher affinity for the receptor, or by raising the intrinsic activity of the hormone-receptor complex (cf. Fig. 1). Many hormones have a broad spectrum of biological action. The search for compounds displaying a dissociation in their action profile is therefore important.

The effect of structural modification on the binding to the receptor has been impressively demonstrated for insulin[40-42]. Various insulin analogs are bound to fat cells or liver cell membranes to a lesser extent than the native hormone, and the biological activity measured *in vitro* usually also decreases. However, the maximum biological effect can always be achieved by using a sufficiently high concentration dependent upon the particular modification. Accordingly, while the affinity for the receptor may change on modification, the intrinsic activity of the receptor complex does not. Studies on insulin were facilitated by the possibility of clear-cut modification of the molecule. Removal of the N- or C-terminal amino acid from the A chain, or of a C-terminal penta- or octapeptide from the B chain leads to a distinct loss of affinity. In contrast, removal of the N-terminal amino acid from the B chain is well tolerated (Fig. 12).

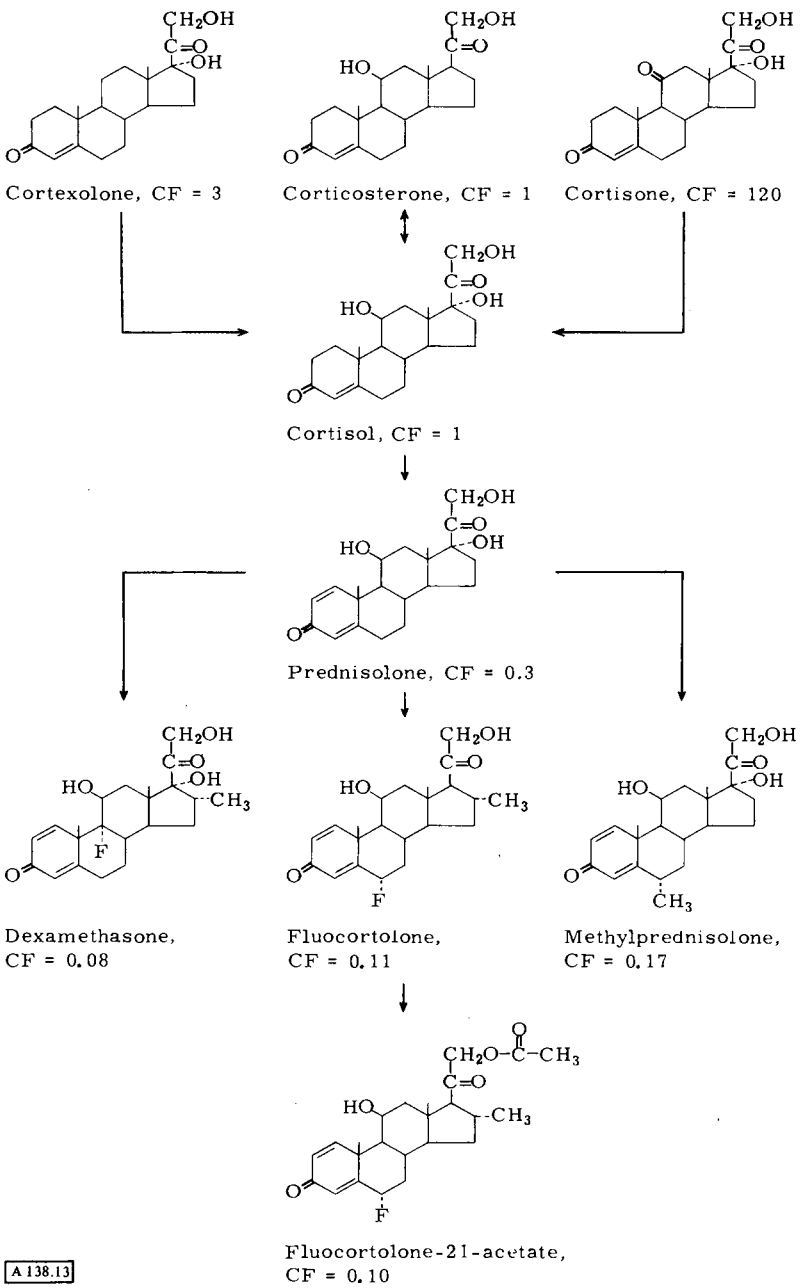

Fig. 13. Binding of glucocorticoids to the receptor (rat thymus). *CF* = competition factor (see Section 3.3).

Substitution of the terminal amino groups or introduction of intramolecular bridges reduces the affinity, but it is not lost entirely. Many of these derivatives nevertheless lead to a pronounced reduction of blood sugar levels *in vivo*. This effect is attributed to the enhanced resistance of the modified molecule towards enzymatic degradation in the liver.

The receptor binding of glucocorticoids will serve as a further example (Fig. 13)[43]. Starting from cortisol, loss of the 11β-hydroxyl group (cortexolone) but not of the 17α-hydroxyl group (corticosterone) reduces hormone binding. Oxidation to the 11-ketone (cortisone) strongly impairs its affinity. The biological activity still observed for 11-oxo corticoids is attributable to their *in vivo* reduction to the 11-hydroxy derivative. Introduction of 1,2-double bond (prednisolone) enhances the affinity towards the receptor. The biological activity also increases. Glucocorticoids exhibiting even stronger binding to the receptor are obtained by introduction of fluorine atoms into the 9α or 6α position. A methyl group in the 16α position also has a favorable effect. Esterification of the 21-hydroxyl function with a short-chain carboxylic acid has practically no effect on binding. Only upon esterification with the longer valeric acid is binding reduced.

Pregnadiene-21-carboxylic esters[44] represent a new class of glucocorticoids. They exhibit moderate to good binding, irrespective of the chain length of the alcohol component. In spite of this affinity, the derivatives are ineffective in all systemic inflammation tests. The reason is to be found in their fast hydrolysis to the free acid which is devoid of receptor affinity (Fig. 14).

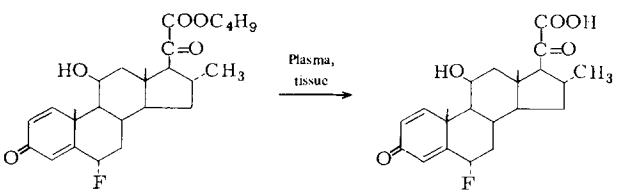

Fig. 14. Locally active corticoid with a labile bond designed to prevent systemic activity.

These compounds deserve considerable interest as local anti-inflammatory agents having practically no systemic side-effects.

7. Outlook

Numerous aspects of hormone-receptor interaction have been investigated since the description of the first receptor protein. However, there still remain many unanswered questions concerning, for example, isolation and characterization of receptor proteins, their amino acid sequence and conformation, and the structure of the receptor molecule as an integral component of the cell membrane. Little is also known about the mechanism of receptor-controlled gene expression and the regulation of receptor biosynthesis.

New findings in all these areas will further our knowledge of hormone action.

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Molecular Aspects of Sickle Cell Disease

By Michael R. Waterman and G. Larry Cottam[*]

Sickle cell hemoglobin (hemoglobin S) contains valine instead of glutamic acid in position 6 of the β-chain. Few detectable conformational differences exist between hemoglobin S and normal adult hemoglobin (hemoglobin A). Following loss of oxygen, sickle cell hemoglobin (hemoglobin S) self associates to form a liquid crystal phase which distorts the erythrocyte into the sickle shape thereby resulting in the clinical symptomology associated with sickle cell anemia. This gel contains deoxyhemoglobin S monomers and polymers in equilibrium. The polymerization process is known to have a negative temperature coefficient, to be pH dependent, and to be extremely dependent on hemoglobin S concentration. The polymerization of deoxyhemoglobin S appears to be entropically driven and occurs in two kinetic phases, a delay period and a rapid polymerization process. The polymer consists of tubules containing six or eight strands of deoxyhemoglobin S tetramers which align with one another. Each strand is wound around the tubule with a pitch of about 3000 Å, but the precise nature of the intermolecular hemoglobin S contacts is not known. Subsequent alignment of the tubules occurs and results in the tactoids observed in (S/S) erythrocytes. While many of the details of polymer formation and structure remain to be elucidated, several attempts to chemically alter the sickling phenomenon have been carried out. As yet, however, no satisfactory chemical treatment has been discovered.

1. Introduction

Sickle cell anemia was first reported in 1910 by *Herrick*[1], who described a patient that had elongated and sickle shaped red blood cells. In an extensive study *Neel*[2] demonstrated that sickle cell disease is inherited in a Mendelian fashion, as previously suggested by *Huck*[3]. *Neel* also explained the existence of clinically benign individuals (sickle cell trait) as being heterozygous for hemoglobin S and individuals with sickle cell anemia as being homozygous for hemoglobin S. However, the first chemical description of the disease and the fact that it was the result of an abnormal hemoglobin molecule awaited the application of electrophoretic techniques, with which *Pauling et al.* in 1949 succeeded in separating the sickle hemoglobin from the normal hemoglobin[4].

In 1957, *Ingram* applied the techniques of peptide mapping to determine the precise chemical differences between hemoglobin A and hemoglobin S. Normal adult hemoglobin (hemoglobin A) contains four polypeptide chains which consist of two identical α-chains of 141 amino acid residues and two identical β-chains which contain 146 amino acid residues ($\alpha_2\beta_2$). *Ingram* was able to demonstrate that hemoglobin S contained a single amino acid substitution different from hemoglobin A. In the β-chain, the amino acid valine has been substituted for glutamic acid six residues from the amino terminus[5]. Except for this one amino acid, all other amino acids in the α- and β-chains of hemoglobin S are identical to those found in hemoglobin A. Thus, hemoglobin S contains two normal α-chains in addition to two abnormal β-chains and is written as $\alpha_2\beta_2^{6\,Glu\rightarrow Val}$. Individuals with sickle cell trait have hemoglobin S and hemoglobin A, while individuals with sickle cell anemia have only hemoglobin S.

The clinical manifestations of sickle cell anemia, *i.e.* the anemia and the acute ischemia and infarction of tissues and, therefore, the chronic loss of organ function, are a consequence of the cell sickling phenomenon. This phenomenon, in turn, has been shown to result from the polymerization of deoxy-

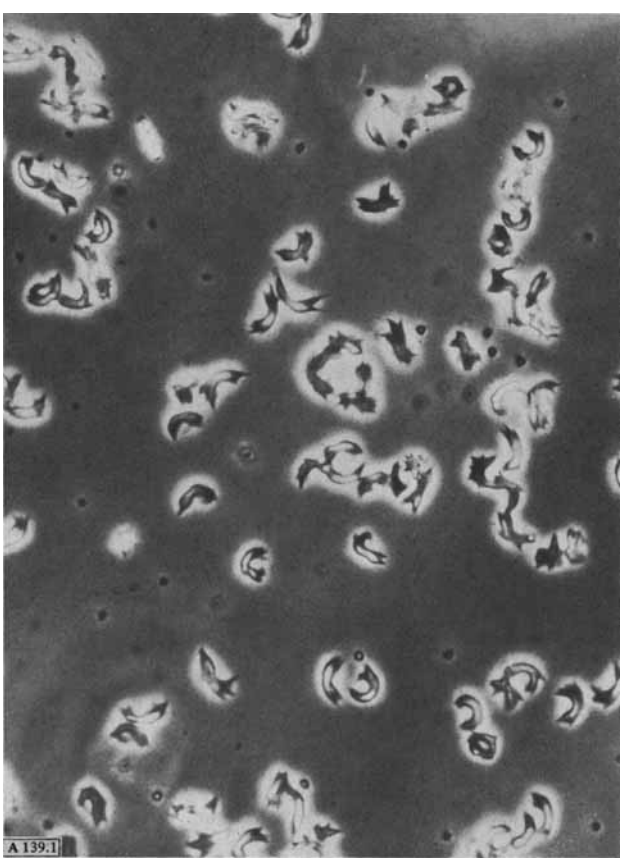

Fig. 1. Microscopic appearance of sickled erythrocytes. Oxygen was removed from these erythrocytes chemically, using a 1 % solution of sodium metabisulfite.

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hemoglobin S molecules[*] inside the erythrocyte. As the hemoglobin S molecules give up oxygen to surrounding tissues, they aggregate into large fibers which distort the erythrocyte membrane into the sickle shape (Fig. 1). The polymerization manifests itself as gel formation. This is in contrast to normal adult hemoglobin which, upon deoxygenation, remains in solution. Sickled cells are less pliable than normal red cells and tend to become trapped in capillary beds, resulting in an occlusion of blood flow and ultimately tissue damage. An enormous amount of clinical literature has appeared on sickle cell anemia over the years and is beyond the scope of this article; however, the reader's attention is drawn to a few recent reviews which have been written on the subject[6-10].

The number of studies on the biochemical and biophysical aspects of sickle cell disease has increased explosively in recent years, particularly in the United States. It is the purpose of this article to review the most pertinent aspects of these works. Due to the great complexity of the polymerization process, much of the work has been phenomenological in nature. However, it is clear that a consistent pattern is developing from several different types of experimental approaches and an understanding of the fundamental structural, kinetic and equilibrium properties of this complicated interaction between protein molecules is emerging. It is hoped that from this understanding a useful clinical regimen will arise for the treatment of this molecular disease.

2. Early Studies of Gelation

Following the elucidation of the primary sequence of hemoglobin S, relatively few biochemical studies were undertaken to determine the nature of the aggregation process until the present decade. Since 1970, the aggregation process has been studied extensively, using numerous physical methods to unravel its complex nature. Some crucial observations made between 1950 and 1970, however, provided a basis for the recent experiments.

The first important observation was made by *Harris*; he found that the viscosity of red cell hemolysates from individuals with sickle cell anemia increases markedly upon deoxygenation. Upon lysing the erythrocytes, he was able to show a concentration-dependent viscosity change following oxygen removal. At high concentrations of hemoglobin S (235 mg/ml), he observed a semi-solid gel-like state which had an optical birefringence similar to that observed in erythrocytes[11]. The gelation, which can be made reversible by the reintroduction of oxygen[12], occurs even in the presence of other hemoglobins such as hemoglobin A[13]. However, a minimal amount of hemoglobin S must be present for gelation to occur (cf. also Table 5). The diagnostic significance of the gelation for identification of hemoglobin S has also been considered.

Another important observation was made by *Itano*. He showed that deoxyhemoglobin S dissolves much more sparingly in 2.24 M phosphate buffer at pH 7.0 than does deoxyhemoglobin A[14]. The reduced solubility of deoxyhemoglobin S in concentrated salt solution has been exploited by several investigators in studying the parameters of the polymerization process[15-17]. In addition, use has been made of this observation in the development of a solubility method for the detection of hemoglobin S in mass screening programs.

In 1957, *Allison* reinvestigated the reported viscosity changes and showed that oxyhemoglobins S and A and deoxyhemoglobin A all had the same viscosity characteristics over a concentration range of 5 to 250 mg/ml and a temperature range of 0 to 40 °C. Deoxyhemoglobin S, on the other hand, behaved quite differently. At concentrations in excess of 120 mg/ml, a sharp increase in viscosity was observed as the temperature of the solution was increased above about 15 °C. On cooling, the viscosity decreased again[18]. The reversibility of the polymerization process by lowering the temperature is an extremely important property which has been exploited in virtually every study since its discovery. Conversely, at any set temperature above *ca.* 15 °C, there is a sharp increase in viscosity as the hemoglobin S concentration is increased (see Table 1).

Table 1. Specific viscosities η_{sp} of aqueous solutions of deoxyhemoglobins A and S as a function of concentration c at 37 °C [18].

Deoxyhemoglobin A		Deoxyhemoglobin S	
c [mg/ml]	η_{sp}	c [mg/ml]	η_{sp}
50	1.5	50	1.5
110	5	100	4.5
200	20	115	5.7
275	41	125	8.5
		130	43.5
		150	gel

A valuable contribution made by *Murayama* was the concept that the negative temperature coefficient of gelation is an indication of the importance of hydrophobic interactions in polymer formation[19]. This is consistent with an amino acid substitution of valine for glutamic acid, and several attempts to design anti-sickling compounds have been based on this concept. In summary, these early studies established that gelation is a highly concerted process dependent on temperature, hemoglobin concentration and oxygen tension.

3. Differences between Hemoglobin S and A

Perhaps the most frustrating aspect of the study of the aggregation of deoxyhemoglobin S is the fact that the physical properties of the hemoglobin S molecules in the polymer appear not to differ from those of the molecules in solution. Careful studies, including the use of polarized absorption spectroscopy[20], have shown that the optical properties of the heme group do not change upon polymerization. Other portions of the molecule have been probed by use of nitroxide spin-labels, and no conformational changes could be observed upon polymerization. The β_{93} cysteine residues have been used as a site of attachment for spin-labels in hemoglobin A to monitor by electron spin resonance the conformational changes which take place during reversible ligand binding[21,22]. When spin-labels were attached to this site in hemoglobin S, the same oxy-deoxy transition as with hemoglobin A could be observed, but no change was observed in going from the deoxy-solution to deoxy-gel state[23]. This result is illustrated in Fig. 2. It follows that the region around the β_{93} cysteine residues in deoxyhemoglobin S is not perturbed upon polymerization and, therefore, that some portions of the surface of the protein remain unaltered. Preliminary

[*] The designation deoxyhemoglobin shall be used here whenever it should be emphasized that deoxygenated hemoglobin is involved.

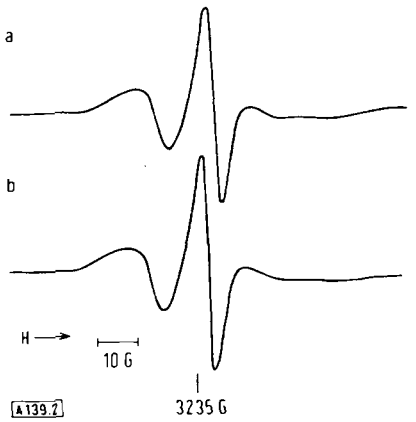
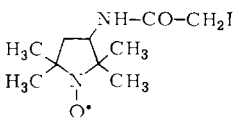
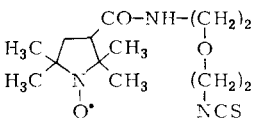


Fig. 2. Electron spin resonance spectra of deoxyhemoglobin S spin-labeled with 3-(2-iodoacetamido)-2,2,5,5-tetramethyl-1-pyrrolidinyloxyl *(1)* at the β_{93} cysteine residues. a) Sample at 53 mg/ml (not a gel), b) sample at 283 mg/ml (a gel). The spectra were recorded at 23°C.

studies in which 3-{[2-(2-isothiocyanatoethoxy)ethyl]carbamoyl}-2,2,5,5-tetramethyl-1-pyrrolidinyloxyl *(2)* was employed for the spin labeling indicate that the N-terminal residues of the β-chains in hemoglobin S are also insensitive to changes which may occur upon aggregation[24]. The



(1)



(2)

enthalpy change in the polymerization process has been estimated to be relatively small, a result which also indicates no large conformational change in the deoxyhemoglobin S molecules during gelation[25, 26]. Needless to say, this inability to find a property of the hemoglobin S molecule which changes upon polymerization has complicated the study of this process.

With respect to differences between hemoglobin S and hemoglobin A, two interesting observations have recently been made. *Asakura et al.* observed that oxyhemoglobin S is very much less stable toward mechanical shaking than is oxyhemoglobin A[27]. This instability is unique for the oxygenated form and, therefore, strongly suggests conformational differences between oxyhemoglobin S and oxyhemoglobin A. Using high-resolution ^{1}H-NMR spectroscopy, *Ho et al.* have detected small pK differences in three surface histidyl residues between deoxyhemoglobin S and deoxyhemoglobin A[28]. The largest of these differences is found to be 0.2 pK unit. The assignment of these residues is not complete, but it is clear that these results reflect localized conformational differences on the surface of the deoxyhemoglobin S molecule with respect to deoxyhemoglobin A. Therefore, it must be concluded that some structural differences exist between hemoglobin S and hemoglobin A in solution, but these differences are subtle and thus far have not been useful as probes for the study of the polymerization process. To date, it has been necessary to take advantage of the changes in the physical characteristics of the solution to study polymerization.

The techniques of immunology may also lead to a better understanding of slight conformational differences between hemoglobin S and hemoglobin A. Recently, the β-chain of hemoglobin S has been used to elicit antibodies[32]. An antibody population with specificity for the N-terminal region of this β-chain was then isolated by affinity chromatography. Cross reactivity with the β-chain of hemoglobin A or hemoglobin α-chains was not observed[33]. This method has potential utility in both the detection and quantification of hemoglobin S, as well as in the study of conformational differences between hemoglobin A and hemoglobin S.

The function of hemoglobin is sensitive to its conformation and thus might provide a tool to distinguish small differences between the two hemoglobins. However, the oxygen binding parameters of dilute solutions of hemoglobin S are indistinguishable from those of hemoglobin A[29]. Differences between oxygen binding parameters of hemoglobin S and hemoglobin A have been observed in whole blood[30, 31]. Blood containing hemoglobin S is found to have a significantly lower oxygen affinity; this is most likely due to the aggregation of deoxyhemoglobin S which tends to stabilize the T (deoxy) configuration, thereby shifting the equilibrium curve to the right. The clinical implications of the relationship between the extent of this shift and various red cell parameters such as volume, hemoglobin concentration and 2,3-diphosphoglycerate concentration are not completely clear. The shifting of the equilibrium curve may well have important consequences with respect to the severity of the disease.

4. Kinetic and Thermodynamic Studies

The kinetics of the sol-gel transition have recently been studied by a variety of methods. Widely different techniques such as viscosity measurements[34, 35], calorimetry[36], and measurement of birefringence[36], turbidity[37], and nuclear magnetic resonance water line widths[38], as well as transverse water proton relaxation times[39] have all shown that there is a delay period prior to the onset of the polymerization process on warming a solution of deoxyhemoglobin S from 4°C to ambient temperature or higher. The gel formation itself follows the delay period and is rapid. The length of the delay period is found to be dependent on the hemoglobin

Table 2. Summary of the kinetic delay times t_d in the polymerization of deoxyhemoglobin S as measured by different techniques.

Method, or property measured	Temperature jump [°C]	Hemoglobin S concentration [mg/ml]	t_d [min]	Ref.
Calorimetry	0→20	233	50	[36]
Optical birefringence	0→20	233	50	[36]
Turbidity	2→30	200	5	[37]
Viscosity	2→25	176	36	[34]
Viscosity	2→21	208	12	[35]
Water proton NMR linewidths	0→21.5	267	10	[38]
Transverse water proton relaxation times	4→37	170	20	[39]

concentration and the temperature to which the system is warmed. The delay time for the polymerization process has been expressed as:

$$1/t_d = \gamma S^n$$

where t_d is the delay time, S is the supersaturation ratio (total hemoglobin S concentration divided by the minimum concentration for gelation) while n and γ are parameters independent of the experimental conditions[36]. The value of the

constant γ is 10^{-6} s. The value of n represents the number of monomers in the nucleation species and is high, at least 30. A summary of the delay times observed by different methods and under different conditions is given in Table 2.

It is possible that different techniques are monitoring different aspects of the overall polymerization process, but a significant delay time is seen in all cases. The length of the delay period is temperature dependent and apparently the reciprocal of the delay time increases logarithmically with increasing temperature[38]. On comparing the temperature dependence of the delay time as determined from optical birefringence, turbidity and reciprocal amplitude of the water proton magnetic resonance line, it was found that all three techniques gave similar results[38]. The length of the delay period is also reciprocally related to a very high power (≈ 30) of the hemoglobin concentration. *Eaton et al.* therefore proposed a model in which the rate determining step is the formation of thermodynamically unstable nuclei of approximately 30 deoxyhemoglobin S molecules[20]. The delay time has important implications clinically and will be discussed later (in Section 7).

From a kinetic standpoint the self association of deoxyhemoglobin S molecules is strongly dependent on hemoglobin concentration and temperature and probably other parameters such as pH. The concentration dependence seems to be manifested in two ways, one being a delay time before the onset of polymerization and the other being the rate at which polymer formation proceeds. Figure 3 shows the water proton

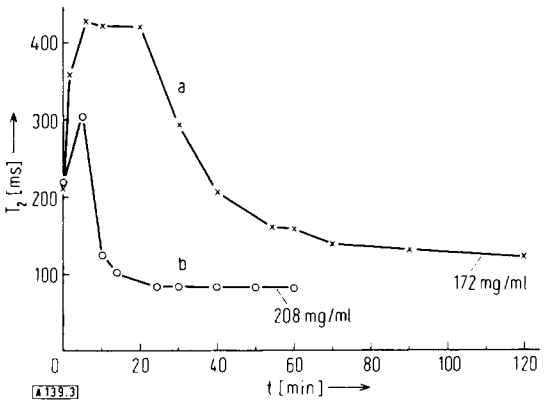


Fig. 3. Transverse water proton relaxation times (T_2) as a function of time at two hemoglobin S concentrations (a: 172 mg/ml; b: 208 mg/ml). The time zero T_2 values were measured at 4 °C and all other T_2 values were measured at 37 °C. The pH in both samples was 7.0; hemoglobin S was maintained in the deoxy form by addition of $Na_2S_2O_4$ [39].

relaxation times (T_2) as a function of time in the polymerization of deoxyhemoglobin S. It can be seen that the delay time t_d decreases greatly with increasing hemoglobin concentration (172 mg/ml: 20 min, 208 mg/ml: 5 min), and the rate of polymer formation increases. It is clear that this concentration dependence is not hemoglobin S specific. In Figure 4 it is seen that by adding 40 mg/ml hemoglobin A to a solution of 170 mg/ml hemoglobin S, the delay time is similarly decreased and the rate of polymerization is increased. The results resemble those obtained with a solution of 208 mg/ml hemoglobin S (Fig. 3b)[39]. The more subtle aspects of the kinetics of hemoglobin S polymerization remain to be elucidated. In particular, investigations on solutions in which hemoglobin S is present in the same concentrations as in erythrocytes have yet to be carried out.

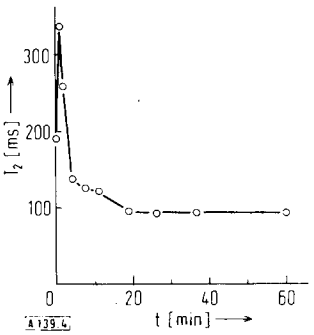


Fig. 4. Transverse water proton relaxation times (T_2) as a function of time in a solution of hemoglobin containing 170 mg ml hemoglobin S and 40 mg ml hemoglobin A. Other conditions were as described for Figure 3 [39].

As pointed out above, the size of the nucleation species has been estimated to contain at least 30 hemoglobin molecules[20]. Studies on the equilibrium properties of the deoxyhemoglobin S system have been largely concerned with the question of whether small aggregates of deoxyhemoglobin S, a few hemoglobin molecules in size, are present in the sol-gel transition. From equilibrium centrifugation studies, contradictory data has been obtained. Observations with a schlieren optical system showed a pre-gelation transition zone which could be ascribed to intermediates[40]. On the other hand, observations with a Rayleigh interferometer provided no evidence for aggregates with less than 20 hemoglobin molecules; hence it is concluded that the polymerization process is a very concerted one[41]. Light scattering studies have indicated that pre-gelation aggregates may exist in solution and that the polymerization process is linear, rather than concerted[42].

From the measurement of spin-lattice relaxation rates of solvent water protons, it has been estimated that about 90% of the deoxyhemoglobin S molecules remain in solution at 10 °C while at 35 °C virtually all are incorporated into the gel[43]. Centrifugation studies indicate that the gel consists of deoxyhemoglobin S monomers in equilibrium with a solid polymer phase[26, 44]. Measurements of longitudinal water proton relaxation times (T_1) have suggested that interactions between oxyhemoglobin S molecules may occur within erythrocytes[45]. Determination of transverse water proton relaxation times (T_2) has been useful in the study of the deoxyhemoglobin S aggregation process and has recently shed some light on the controversy surrounding pre-gelation aggregates[46–49]. In this technique, the T_2 value is monitored as a function of time (see Fig. 3 and 4). The technique is applicable to both intact erythrocytes and isolated hemoglobin solutions[46]. It has been used, for example, to study the influence of pH[48] and potential anti-sickling agents[50] on the polymerization process. In order to explain the observed drop in T_2 the three water environment model was proposed[47]: free water, water of hydration, and irrotationally bound water. Table 3 summarizes the model in terms of the mol fractions of water in each environment and its characteristic correlation

Table 3. Three water environments inside intact erythrocytes [47].

Water Environment	Mol Fraction	Correlation Time τ_c [s]
Free Water (Bulk Water)	0.98	3×10^{-11}
Water of Hydration	0.013 0.015	$2\ 4 \times 10^{-9}$
Irrotationally Bound Water	0.002	$\geq 10^{-7}$

time τ_c. Upon polymerization the correlation time of the "irrotationally" bound water fraction increases and gives rise to the observed decrease in relaxation time T_2. Thus the reduced T_2 value is a function of the degree of polymerization in the deoxyhemoglobin S solution.

One must now ask how high the degree of polymerization must be in order to yield the observed changes in T_2? This has been approached by assuming a linear polymer model and calculating the expected correlation times for comparison with those actually observed in solutions of deoxyhemoglobin S[49]. The correlation time of oxyhemoglobin S is 2.23×10^{-8} s, while that observed for polymerized deoxyhemoglobin S is 2.64×10^{-7} s[49]. It can be seen from Table 4 that a linear association of from one to seven hemoglobin S molecules can yield the range of observed correlation times. Thus, the measurement of transverse water proton relaxation rates is sensitive to the initial events of polymerization. This result is supported by the fact that with S/S erythrocytes, an *n*-value of 2.5 is obtained when the change in T_2 is measured as a function of oxyhemoglobin concentration and expressed as a Hill plot. Therefore, in this special case the deoxygenation of hemoglobin can be measured by this technique[49]. Since the onset and rate of polymerization are very concentration dependent, it may be assumed that intermediate states do exist and an understanding of their formation and disappearance is essential to an overall understanding of the polymerization process.

Table 4. Calculated correlation times for linear polymerization of deoxyhemoglobin S [49]. Calculations were made assuming hemoglobin as a sphere of 64 Å diameter. The degree of association gives the number of molecules in the linear polymer and is also the axial ratio.

Degree of Association	τ_c [s]
1	2.23×10^{-8}
2	5.20×10^{-8}
3	9.14×10^{-8}
4	1.35×10^{-7}
5	1.81×10^{-7}
6	2.26×10^{-7}
7	2.75×10^{-7}

Thermodynamic measurements do not rule out the existence of small polymers. The enthalpy of polymerization is 2—4 kcal/mol[25, 26] and the increase in entropy of about 25 cal/K^{-1} mol^{-1} at 20°C is considered to be the driving force for the reaction[26]. This entropy change is smaller than described for some other biological polymerization processes and is compatible with the existence of stable, small polymers[26].

Minton has proposed a two-step thermodynamic model for the gelation of hemoglobin S[51–54]. In this model, deoxyhemoglobin S molecules exist in the monomer form until a critical concentration is attained. Above this concentration rod-like microtubules form by a process which is thermodynamically equivalent to precipitation. The rod-like aggregates then spontaneously align to form the gel when their volume fraction exceeds a critical value. The critical volume fraction is sensitive to the length of the rod-like forms in solution; the longer the rod length, the lower the volume fraction necessary for alignment. This model is reported to be consistent with experimental observations and has been applied to both the chemical inhibition of gelation and the influence of oxyhemoglobin S on the gelation process.

In summary, the aggregation of deoxyhemoglobin S is a concentration- and temperature-dependent process consisting of several discernable steps whose driving force is the increase in entropy. Kinetically, there is a delay period before the polymerization begins. During this delay period there appears to be no formation of stable small polymers. In contrast, however, stable small polymers apparently are formed during the aggregation phase of the overall process, and they serve as precursors to the nucleation species which is larger than 30 hemoglobin molecules. In the light of what is known concerning the structure of the polymer described in the next section, there must be kinetic processes such as the alignment of tubules which remain to be sorted out from the overall process.

5. Structure of Crystals and Fibers

Considerable interest has been focused on the structure of the deoxyhemoglobin S polymer. It is anticipated that by understanding the fiber structure, and in particular the intermolecular amino acid contacts, it might be possible to design a specific anti-sickling agent. Considerable detail concerning the fiber structure has been obtained from electron microscopy (Fig. 5). This technique has shown that deoxyhemoglobin S in erythrocytes and in isolated solution forms tubules having an outside diameter of about 170 Å[19, 55, 56]. These studies show that fibers are formed by alignment of the tubules with each other. Early studies by *Finch et al.*[57] and *Edelstein et al.*[58] produced evidence that the tubule is made up of rings of six hemoglobin tetramers stacked on top of each other with a helical pitch to the arrangement of rings. In the two studies noted above, there were differences in the helical pitch and the alignment of tubules, but the model stemming from these studies showed that there are three kinds of intermolecular hemoglobin contacts which result in fiber formation. These are up-down within the tubule, resulting in the long axis of the tubule; side-side within the tubule, resulting in the ring structure of the tubule; and interactions between the tubules, resulting in alignment and therefore fiber formation. Recent electron microscopy studies suggested that the tubules are eight-stranded (Fig. 6), rather than six-stranded, and that the adjacent strands in the tubule long axis are staggered with respect to each other by half the repeat distance[59].

It is not known at present which amino acids are involved in these interactions; however, some information is available concerning contact points between deoxyhemoglobin S molecules. X-ray diffraction patterns have been obtained from deoxyhemoglobin S gels[60] and recently the 5 Å and 3 Å X-ray structures of deoxyhemoglobin S crystals have been determined[61, 62]. It is interesting that much of the data from the 3 Å X-ray study is in good agreement with the electron microscopic data and other information known about fiber structure. For example, in 1973 *Hofrichter et al.* established, by measuring absorption of polarized light, the maximum angle (23°) which could exist between the tubular axis and the molecular *x* axis[20]. In the crystal, this angle is less than 10°. In addition, several of the known sites which affect the gelation process are found to be intermolecular contacts in the crystals. For example, one of the β_6 residues is involved in the side-side contacts, as is one of the β_{73} residues. In

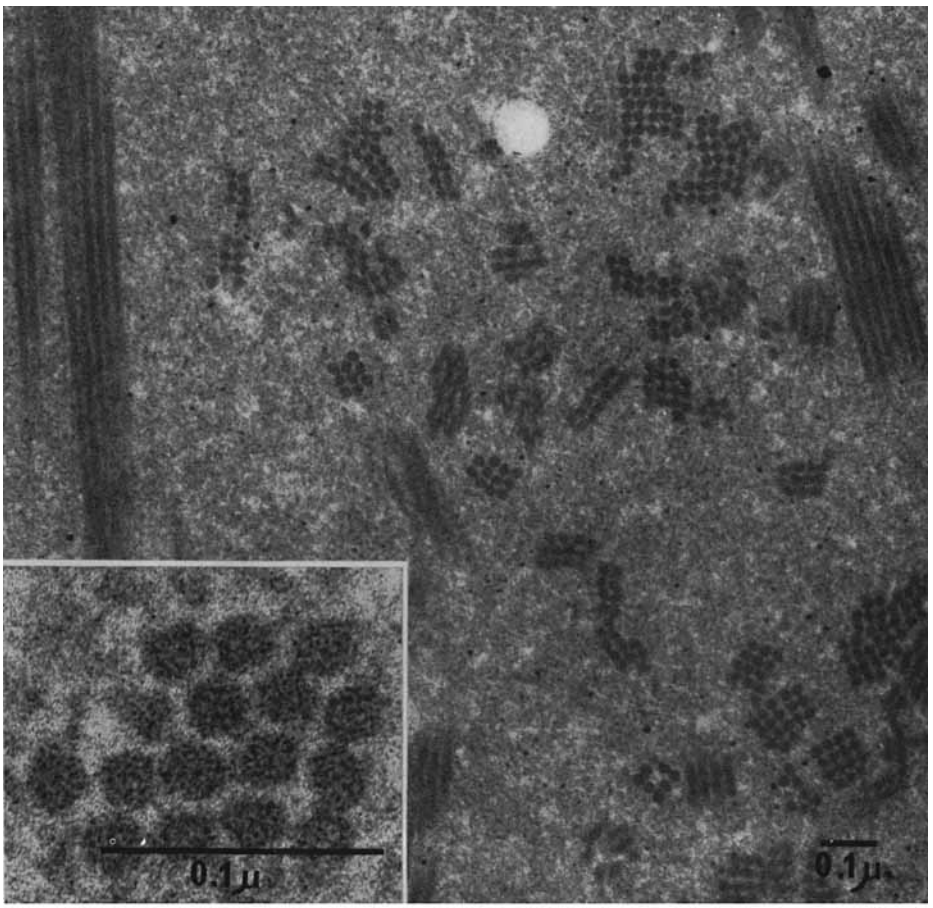


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Fig. 5. Transmission electron micrograph of hemolysate from S/S erythrocytes upon deoxygenation showing both the longitudinal and transverse sections of the fibers from Ref. [69].

hemoglobin C_{Harlem}, there is an Asp→Asn substitution at β_{73} in addition to the Glu→Val substitution at position β_6. This results in an increased concentration necessary for gelation to occur[63]. Several other sites which have been suspected of being involved in intermolecular contacts from studies with abnormal hemoglobins are also implicated in the crystallographic data. Furthermore, the structure of deoxyhemoglobin S does not differ significantly from that of deoxyhemoglobin A in the β_6 region. From crystallographic data a model tubule can be constructed which has many similarities with the eight-stranded model described above. It is also suggested that the tubule consists of double strands in which the molecules are staggered by half the repeat distance[62].

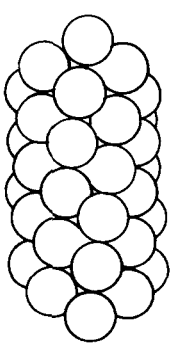

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Fig. 6. Model of eight-stranded deoxyhemoglobin S fiber along the longitudinal axis, as suggested from X-ray and electron microscopy studies [59, 62]. Each circle represents a single molecule of deoxyhemoglobin S.

Further studies on the mapping of the intermolecular contact points have been carried out using hybrid hemoglobins consisting of mutant α-chains and hemoglobin S β-chains[17]. In these studies, the solubilities of the hybrid hemoglobins have been measured in order to assess the influence of the α-chain abnormalities on the polymerization process. The results appear to be consistent with those derived from X-ray crystallography and electron microscopy. In addition, they have been found, in part, to be consistent with the computer modeling approach to the determination of the intermolecular contact points[64].

While many details of the deoxyhemoglobin S fiber remain to be determined, it is clear that the fiber consists of tubules made up of strands of deoxyhemoglobin S molecules. The contacts between molecules and between strands probably do not involve many amino acids so that much of the surface of the hemoglobin molecule is free to the solvent. The forces which result in tubule formation do not change the measurable properties of the hemoglobin molecules. However, the tubular fibers which are formed are sufficiently stable thermodynamically to force the erythrocyte membrane into the sickled shape.

6. Non-Gelling Hemoglobins

It is well recognized that while homozygosity for hemoglobin S (sickle cell anemia) is often associated with severe clinical symptomology, heterozygosity for hemoglobin S (sickle cell

trait) is a clinically benign state. Therefore, non-gelling hemoglobins, such as hemoglobins A and F, have been extensively studied for their effect on the polymerization process[13, 65, 66].

Expanding on the original work of *Singer* and *Singer*[13], *Bookchin* and *Nagel* have developed a widely-used technique for this type of study. In these experiments, the minimum gelation concentration (MGC) is measured under a specific set of conditions (0.15 M phosphate buffer, pH 7.35, 25°C), the MGC being the concentration of hemoglobin below which no gelation will occur. By using a constant set of conditions, it is possible to study not only the effect of non-gelling hemoglobins on the MGC, but also potential anti-sickling agents and mutations in the hemoglobin S molecule at positions other than β_6.

Table 5. Effect of non-gelling hemoglobins (Hb) on the MGC [60, 61] of deoxyhemoglobin S. The normal hemoglobin concentration in the erythrocytes is 320 to 340 mg/ml.

Hemoglobin composition	MGC [mg/ml]
100 % HbS	235–248
50 % HbS + 50 % HbA	301
50 % HbS + 50 % HbF	353–366
100 % HbC_{Harlem} [a]	362
50 % HbS + 50 % Hb Korle-Bu [b]	355–361

[a] HbC_{Harlem} contains two substitutions in the β-chain ($\beta_6^{Glu\rightarrow Val}$ and $\beta_{73}^{Asp\rightarrow Asn}$).
[b] Hb Korle-Bu contains one substitution in the β-chain ($\beta_{73}^{Asp\rightarrow Asn}$).

In Table 5, the effect of non-gelling hemoglobins on the MGC of hemoglobin S is shown. As can be seen, both hemoglobins A and F substantially increase the MGC, hemoglobin F being more effective than hemoglobin A. In addition, the substitution of Asp→Asn at β_{73} also significantly increases the MGC. An equal amount of hemoglobin A raises the MGC to approximately the hemoglobin concentration inside the erythrocyte, while hemoglobin F raises this concentration above that found in erythrocytes. Therefore, while cells which contain hemoglobins A and S in approximately equal concentration are known to sickle upon complete deoxygenation *in vitro*, they probably never experience a low enough oxygen concentration *in vivo* to sickle. Hence, the normal sickle trait hemoglobin profile (45 % hemoglobin S and 55 % hemoglobin A) is a benign condition clinically. Another point to be drawn from Table 5 is that an amino acid substitution far from the β_6 position can have a profound influence on the MGC. This is due to the multiple amino acid contacts which are necessary for fiber formation.

The mechanism by which non-gelling hemoglobins change the MGC is unknown. However, hybrid tetramers ($\alpha_2\beta_A\beta_s$) have been observed in mixtures of hemoglobin A and hemoglobin S[67], and it has been shown experimentally that under conditions where hybrid tetramers can form, the MGC is increased, but not to the level observed under conditions where hybrid tetramers are not present[68]. Therefore, non-gelling hemoglobins may be incorporated into the fiber structure in two ways, as complete tetramers and as hybrid tetramers; the latter combination results in an increase in the MGC but still permits gelation to occur[69]. Certainly, the possible role of hybrid tetramers in gel formation in hemoglobin mixtures deserves further consideration.

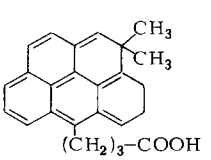
However, the effect of non-gelling hemoglobins increasing the MGC is not sufficient to explain the clinical differences between sickle cell anemia and sickle cell trait. The hemoglobin concentration in normal erythrocytes ranges between 320 and 340 mg/ml. From Table 5 it is clear that 50 % hemoglobin F instead of 50 % hemoglobin A would be very advantageous, since it raises the MGC above the normal red cell hemoglobin concentration. The occurrence of 50 % hemoglobin F, however, is extremely rare. On the other hand, 50 % hemoglobin A also raises the MGC, but not above the normal red cell hemoglobin concentration. It is estimated that between 8 and 10 % of the black population in the United States have about 45 % hemoglobin S and 55 % hemoglobin A (sickle cell trait), and the erythrocytes from these individuals are known to sickle following complete removal of oxygen. Therefore, hemoglobin A must have another role in addition to raising the MGC.

It has recently been shown using the measurement of water proton relaxation times, that polymerization occurs immediately and concomitantly with deoxygenation in S/S erythrocytes[49]. In heterozygous erythrocytes (A/S or C/S) there is a delay in the onset of polymerization until a critical level of deoxyhemoglobin is achieved. The critical level of deoxyhemoglobin is dependent on the amount of hemoglobin S present in the erythrocytes, the more hemoglobin S the lower the level of deoxyhemoglobin necessary for the onset of polymerization.

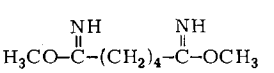
Therefore, non-gelling hemoglobins play at least two important roles in the polymerization process which must, in part, be responsible for the clinically benign state of sickle cell trait. They increase the MGC and they increase the level of deoxygenation which must be achieved before the onset of the polymerization process. It is also anticipated that non-gelling hemoglobins will prove to alter the kinetics of the polymerization process in a favorable manner, *i.e.*, slow down the rate of polymerization.

7. Chemical Alteration of Gelation

An important goal in the study of the molecular aspects of deoxyhemoglobin S polymerization is to find a chemical solution to this serious and widespread disease. In view of what is known about polymerization, several different compounds have been studied as potential anti-sickling agents. The chemicals studied can be classified into two categories; those which covalently modify hemoglobin S and those which non-covalently alter the polymerization process. Examples of the non-covalent modifiers are urea[70], organic solvents[71], alkylureas[72], amino acids such as lysine, arginine, and aspartic acid[73], and 2,2-dimethyl-3,4-dihydro-2*H*-benzo[*c*,*d*]pyrene-6-butyric acid *(3)*[74]. While these compounds, which do



(3)



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not form covalent derivatives of hemoglobin S, represent various degrees of potency as anti-sickling agents *in vitro*, there is no conclusive evidence that any of them reduce the clinical symptoms associated with the disease. In several cases, the toxicity of the compound has yet to be determined.

The covalent modifiers which have been studied most extensively are cyanate[75-77], carbamyl phosphate[78] and the bifunctional cross-linking agent, dimethyladipimidate *(4)*[79]. While the toxicity of the latter two compounds has yet to be clearly established, the studies with cyanate are extensive and illustrate the two major problems of covalent modification: it is difficult to covalently modify only hemoglobin *in vivo*, and moreover to do so without impairing the oxygen delivery function of hemoglobin. Therefore one may want to modify only a few of the total number of amino acids of a specific type. For instance, in cyanate treatment of erythrocytes, cyanate was found to be incorporated to a large degree into the hemoglobin, predominately at the amino terminal valine residues. Yet a small amount of cyanate is bound to other proteins resulting in deleterious clinical side effects, particularly in the nervous system and the eye. As recently discussed by *Manning*[80], many principles have been derived from studies on the carbamylation of hemoglobin S which should also apply to other studies where covalent modification of hemoglobin is attempted. Carbamylation of hemoglobin S occurs primarily at the amino terminal valine residues with the α-chain residues reacting faster than β-chain residues. The anti-sickling effect of cyanate seems to result from two quite different effects. Modification at the α-chain amino terminal residues produces a hemoglobin which has a higher affinity for oxygen and therefore polymerization of this modified hemoglobin S will only occur at lower oxygen tensions[81]. On the other hand, carbamylation of the β-chain amino terminal residues significantly increases the MGC of hemoglobin S[81]. Therefore, a covalent modification can have multiple effects on the polymerization process.

To date, no chemical modifier of the polymerization process has been found which would be useful in the general clinical treatment of sickle cell anemia. This is not to say, however, that such a compound does not exist, and the search for an agent to specifically inhibit or slow down the gelation phenomenon will continue at an accelerated rate as more information becomes available about the biochemical aspects of the process.

The above mentioned compounds have been studied because they have the potential to prevent cell sickling under the conditions of reduced oxygen tension. *Eaton et al.* have recently presented the interesting hypothesis that one approach to reducing the clinical severity of sickle cell anemia is to control the delay time observed in kinetic studies[82]. It is possible that the delay time could be lengthened by some treatment such that it would become longer than the time required for red cell transit through the blood circulation (≈ 15 s). Under these circumstances, reoxygenation of hemoglobin S would serve as the anti-sickling process. This hypothesis opens up fruitful areas of both clinical and basic research as to the role of the delay time in the clinical severity of the disease and the perturbations of the hemoglobin environment which are effective in lengthening the delay time.

The ultimate answer to the problem of sickle cell anemia may lie in the elucidation of the mechanism by which the switch from fetal hemoglobin (hemoglobin F) synthesis to adult hemoglobin synthesis takes place. Since the capacity to synthesize fetal hemoglobin is present in adults, it may be possible some day to turn on synthesis of this hemoglobin, thereby producing heterozygous S/F trait individuals from homozygous S/S individuals. Since sickle cell trait is a clinically benign condition, considerable effort will be invested in this direction in future years.

8. Conclusion

The authors hope that this rather selective review will provide chemists with an insight into the chemical events which are responsible for the clinical symptoms associated with sickle cell anemia. In addition to the problems remaining to be solved, it is hoped that the reader has gained an appreciation for the vigor with which these problems are being tackled in many different laboratories. It is not overly optimistic to anticipate that the structural, kinetic and equilibrium properties of the self association of deoxyhemoglobin S will be much better understood by the end of the present decade and that a chemical solution to the problem will be in sight. In fact it is likely that the treatment of the disease will go through several different phases, each arising because of new advances in the areas of biochemical and biophysical aspects of hemoglobin S.

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COMMUNICATIONS

Conformational Studies on Twelve-Membered Heterocycles. Crystal Structure of 5,18-Dimethyl-5,18-diazatribenzo[*a*,*e*,*i*]cyclododecene-6,17(5*H*,18*H*)-dione

By *W. David Ollis, Julia Stephanidou Stephanatou, J. Fraser Stoddart, Andrew Quick, Donald Rogers*, and *David J. Williams*[*]

The synthesis and conformational behavior of the *N*,*N*′,*N*″-trimethyl[1] and *N*,*N*′,*N*″-tribenzyl[2] derivatives of trianthranilide have been described recently. We now discuss the confor-

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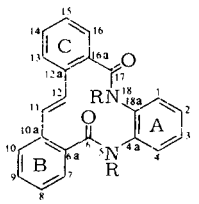
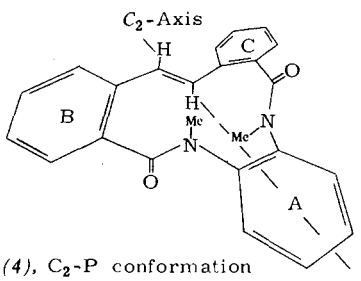
mational properties of the *N,N'*-dimethyl *(2)* and the *N,N'*-dibenzyl *(3)* derivatives of the twelve-membered olefinic bislactam *(1)*[3]:

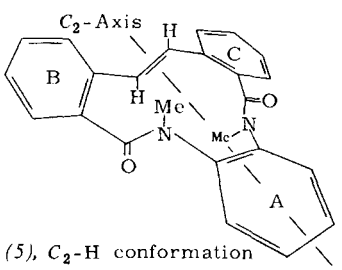


(1), R = H
(2), R = CH_3
(3), R = CH_2-C_6H_5

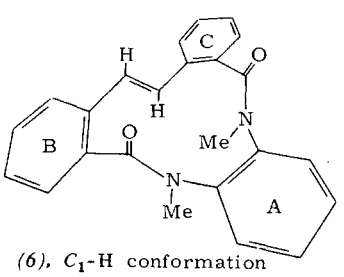
The ^{1}H-NMR spectrum of *(2)* in $CDCl_3/CS_2$ (1:1) at +20°C exhibited singlets at $\tau = 2.90$ and 6.85 for the olefinic and *N*-methyl protons, respectively. No change occurred in the spectrum on cooling the solution to −90°C.



(4), C_2-P conformation



(5), C_2-H conformation



(6), C_1-H conformation

There are three possible non-planar chiral conformations [*(4)*, *(5)*, and *(6)*] to consider for *(2)* which retain two *trans*-amide linkages and the *trans*-olefinic bond [C(11)—C(12)]. The C_2-propeller conformation *(4)* has an approximately parallel alignment of the *trans*-olefinic bond with ring A. In contrast, in the C_2-helix conformation *(5)*, the *trans*-olefinic bond is approximately orthogonal to ring A. The interconversion between the C_2—P *(4)*, C_2—H *(5)*, and C_1—H *(6)* conformations and their enantiomers (C_2—P*, C_2—H*, and C_1—H*) is described by the conformational itinerary given in Figure 1 which includes two pairs of degenerate C_1-helical conformations *(6)* labeled (C_1—H1 and C_1—H2) and (C_1—H1* and C_1—H2*).

These considerations and the ^{1}H-NMR spectroscopic evidence show that *(2)* exists in solution as either (i) inverting C_2—P *(4)*, (ii) inverting C_2—H *(5)*, (iii) rapidly interconverting C_2—P *(4)* and C_2—H *(5)*, or (iv) rapidly inverting C_1—H1 or C_1—H2 *(6)* conformations. Possibilities (iii) and (iv) necessitate rapid re-orientation of the *trans*-olefinic bond at

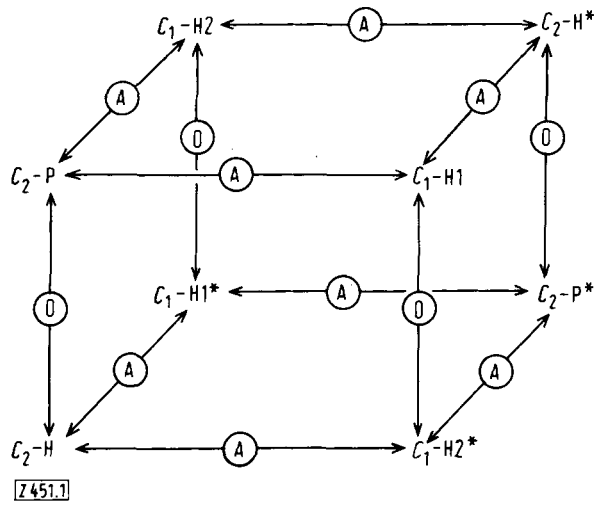


Fig. 1. Conformational changes in derivatives of *(1)*. Ⓐ≡ *trans*-Amide bond re-orientation. Ⓞ ≡ *trans*-Olefinic bond re-orientation.

−80°C: such a process is expected to be slow on the ^{1}H-NMR time scale. However, even if (iii) or (iv) are excluded on the basis of essentially negative evidence, then a decision between (i) and (ii) is still not possible on the basis of ^{1}H-NMR spectroscopy alone. An X-ray crystallographic investigation was therefore undertaken to determine the solid state conformation of the bislactam *(2)*.

(2) crystallizes from methanol as well-formed parallelopipeds. They are orthorhombic $Pna2_1$, $a = 10.708$, $b = 28.233$, $c = 6.197$ Å, $Z = 4$ (2 right-handed, 2 left-handed). Intensities of 1993 reflections were measured on a Siemens diffractometer with $Cu_{K\alpha}$ radiation ($\theta \leq 71°$) and, of these, 18 were reckoned unobserved. The structure was solved by direct methods and refined to a current *R* value of 0.053 showing (Fig. 2) that the molecule adopts a distorted C_2—P conformation *(4)*.

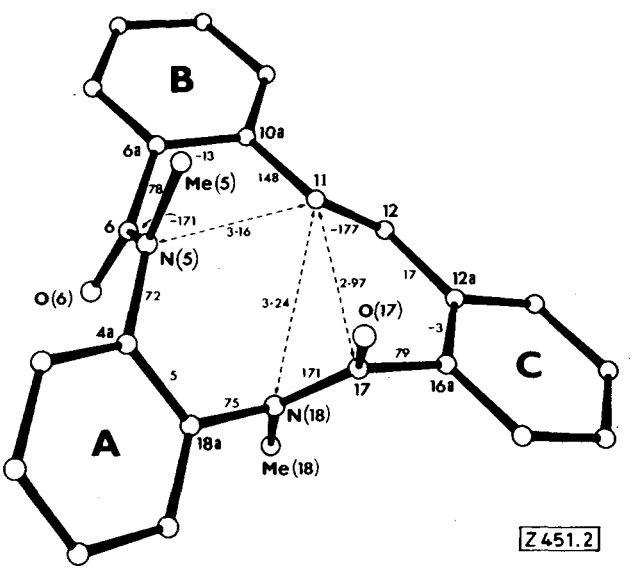


Fig. 2. Torsional angles [°] and some interatomic distances [Å] in the 12-membered ring of the *N,N'*-dimethyl bislactam *(2)*.

The angles between the rings A, B, and C are 35° (A and B), 33° (A and C), and 13° (B and C). The torsional angles (see Fig. 2) show that the planes of the two NMe—CO groups lie roughly perpendicular to the aromatic rings with their *N*-methyl groups on opposite sides of the twelve-membered ring. The olefinic carbon, C(11), protrudes into the twelve-membered ring so as to be nearly equidistant from N(5) and N(18) (3.16 and 3.24 Å, respectively) and only 2.97 Å from C(17).

This distortion of the C_2-propeller conformation *(4)* destroys the molecular C_2-axis and is undoubtedly due to the conjugational demands satisfied by an approach towards a planar stilbenoid grouping in the molecule. The bond angles [129° at C(11) and 126° at C(12)] are very similar to the average of 126.2° found in the recently redetermined structure of *trans*-stilbene[4]. The remainder of the molecule constitutes an asymmetric arrangement around the *trans*-olefinic bond giving torsional angles of 32° and 17° along the C(10a)—C(11) and C(12)—C(12a) bonds, respectively.

The ^{1}H-NMR spectrum of *(3)* in $CDCl_3$ at +20°C exhibits an AB system ($\tau_A = 5.30$, $\tau_B = 5.47$, $J_{AB} = 14.8$ Hz) for the *N*-benzylic methylene protons. When the temperature-dependence was examined in CD_3SOCD_3, the AB system coalesced to give a singlet at +134°C. The rate constant of 94.5 s^{-1}, calculated at the coalescence temperature[5], corresponds to a $\Delta G^{\neq}$ of 20.4 kcal/mol for ring inversion. This is most likely to involve C_2—P$\rightleftharpoons$$C_2$—P* inversion, assuming that the compounds *(2)* and *(3)* are both associated with a preference for the propeller-type conformation *(4)*.

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CAS Registry numbers:
(1), 59247-24-4; *(2)*, 59247-25-5; *(3)*, 59247-26-6

[1] *W. D. Ollis, J. A. Price, J. S. Stephanatou*, and *J. F. Stoddart*, Angew. Chem. *87*, 169 (1975); Angew. Chem. Int. Ed. Engl. *14*, 169 (1975); *W. D. Ollis, J. F. Stoddart*, and *I. O. Sutherland*, Tetrahedron *30*, 1903 (1974).

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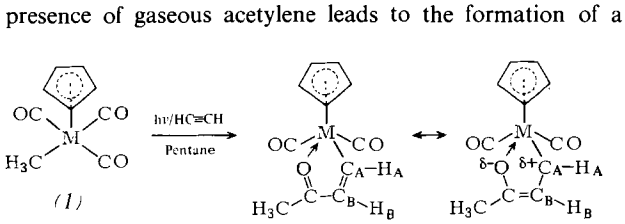
The Photochemical Addition of Acetylene to Tricarbonyl(η^5-cyclopentadienyl)methylmolybdenum and -tungsten

By *Helmut Guido Alt*[*]

The irradiation of transition-metal carbonyls in the presence of potential ligands usually leads *via* cleavage of a CO group to substitution products[1]. In this communication a photoinduced addition of acetylene to $C_5H_5M(CO)_3CH_3$ *(1)* (M = Mo, W) is reported in which the metallocyclic complex of type *(2)* is formed.

The UV irradiation of a pentane solution of *(1)* in the presence of gaseous acetylene leads to the formation of a red, diamagnetic compound *(2)* of formal composition $C_5H_5M(CO)_2(C_2H_2COCH_3)$ (M = Mo, W) as main product. It had been expected from the stoichiometry of the reaction that *(2)* should contain a π-bonded acetylene ligand as well as a σ-bonded acetyl group. Indeed, complexes of the type $C_5H_5M(CO)_2L(COCH_3)$ (M = Cr, Mo, W) are formed, when $C_5H_5M(CO)_3CH_3$ is allowed to react photochemically or thermally with ligands L (*e.g.* triphenylphosphane, trimethyl phosphite)[2]. Spectroscopic characterization of *(2)*, however, revealed that acetylene is not incorporated in the complex simply as a monodentate π-ligand (L).



(1) *(2)*

(a): M = Mo
(b): M = W

Spectroscopic findings are consistent with the formation of a five-membered metallocyclic ring in *(2a)* and *(2b)*. In each case the IR spectrum (in pentane solution) contains two ν(C≡O) absorptions (at 1980, 1905 and 1972, 1897 cm^{-1}, respectively) corresponding to the two CO ligands. The solid-state spectra (KBr) of *(2a)* and *(2b)* exhibit a new band (at 1488 and 1470 cm^{-1}, respectively), which is assigned to the ketonic C=O stretching vibration[3].

The ^{1}H-NMR spectra show singlets for the C_5H_5 and the CH_3 protons. The "acetylene" pattern is shifted very strongly downfield and is split into an AB system; the doublet at low field is assigned to the proton H_A. From the difference in the chemical shifts of H_A and H_B ($\Delta\delta \approx 5$ ppm) it can be concluded that the two protons of the C_2H_2 unit must be in very different environments. Similarly strongly deshielded protons are also observed in the formal acetylene complex $Mo(S_2PR_2)_2(CO)(C_2H_2)$[4], for which the presence of a metallocyclic three-membered ring has been discussed. The coupling constants $J(H_AH_B)$ in *(2a)* and *(2b)* are characteristic for *cis* olefinic protons. Measurements on *(2b)* in [D_8]toluene show no change in the AB system up to 110°C, thus indicating hindered rotation of the acetylene ligand[5].

^{1}H-NMR spectra (in [D_6]acetone; all δ-values in ppm rel. to TMS int.):

	$\delta(C_5H_5)$	$\delta(CH_3)$	$\delta(C_2H_2)$ [H_A/H_B]	$J(H_AH_B$ [Hz]
(1a)	5.59	0.36	—	—
(1b)	5.72	0.42	—	—
(2a)	5.59	2.43	12.01, 7.20	8.6
(2b)	5.70	2.46	12.20, 7.20	9.6

^{13}C-NMR spectra (in [D_6]acetone; all δ-values in ppm rel. to TMS int.):

	δ(M—CO)	$\delta(C_2H_2)[C_AC_B]$	δ(C=O)	$\delta(C_5H_5)$	$\delta(CH_3)$
(2a)	248.35	247.05, 131.73	201.96	93.75	24.38
(2b)	239.18	237.67, 131.72	200.02	92.89	22.98

The unusually strong polarization of the two olefinic carbons in *(2)* is confirmed by the ^{13}C-NMR spectrum, which, in the case of *(2b)* shows an additional ^{13}C-^{183}W coupling of the α-C atom of the five-membered ring with the central atom (73 Hz) besides the ^{13}C-^{183}W coupling of the two terminal CO ligands (154 Hz). Together with the observed chemical shifts this finding affords unequivocal assignment of C_A and C_B.

The photoreactions of *(1)* with methylacetylene, phenylacetylene, and diphenylacetylene likewise lead to metallocyclic complexes[2b].

Experimental:

All operations are carried out under argon and with anhydrous solvents. A solution of *(1)* (3 mmol) in pentane (300 ml) is irradiated for 30 min with a mercury high-pressure lamp (Hanovia L-450W), a slow stream of acetylene being passed

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through the reaction solution at the same time. The dark red-brown suspension that is formed is concentrated by evaporation and the oily residue chromatographed with benzene on silica gel. The first (red) zone contains *(1)* and small amounts of an unknown by-product, the second (orange zone) the complex *(2)*. Recrystallization from pentane at −79 °C affords analytically pure, cherry-red crystals. Yield: 0.077 g (9 %) *(2a)*, m.p. 65 °C; 0.056 g (5 %) *(2b)*, m.p. 74 °C.

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CAS Registry numbers:
(1a), 12082-25-6; *(1b)*, 12082-27-8; *(2a)*, 60410-65-3; *(2b)*, 60410-66-4; HC≡CH, 74-86-2; ^{13}C, 14762-74-4

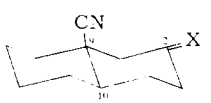
[1] *E. Koerner von Gustorf* and *F. W. Grevels*, Fortschr. Chem. Forsch. *13*, 366 (1969); *M. Wrighton*, Chem. Rev. *74*, 401 (1974).
[2] a) *K. W. Barnett* and *D. W. Slocum*, J. Organomet. Chem. *44*, 1 (1972); b) *H. G. Alt*, unpublished results.
[3] Further evidence in support of this assumption has in the meantime been obtained from studies on the analogous 2-butyne complex: *J. L. Davidson, M. Green, J. Z. Nyathy, C. Scott, F. G. A. Stone, A. J. Welch*, and *P. Woodward*, J. Chem. Soc. Chem. Commun. *1976*, 714.
[4] *J. W. McDonald, J. L. Corbin*, and *W. E. Newton*, J. Am. Chem. Soc. *97*, 1970 (1975).
[5] *M. Herberhold, H. Alt*, and *C. G. Kreiter*, J. Organomet. Chem. *42*, 413 (1972); *J. A. Segal* and *B. F. G. Johnson*, J. Chem. Soc. Dalton *1975*, 1990.

Partial Asymmetric Diels-Alder Reaction with an α-Chloronitroso Compound

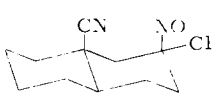
By *Helmut Nitsch* and *Günter Kresze*[*]

In non-catalyzed Diels-Alder reactions of open-chain or cyclic dienes with acrylates, fumarates or glyoxylates of optically active alcohols, the optical yields are generally low (≤ 13 %). We report here on a heterodienophile whose cycloadditions with 1,3-dienes are more selective.

Reaction of the oxime *(2)* (m.p. 140 °C) of 9-cyano-*trans*-2-decalone *(1)*[1] with *tert*-butyl hypochlorite affords a 2-chloro-2-nitroso-9-cyanodecalin *(3)* (m.p. 69 °C; 60 % yield), in which

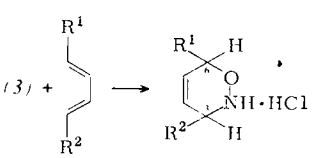


(1), X = O
(2), X = NOH



(3)

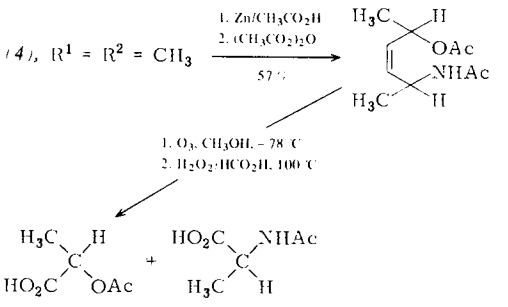
the NO group is axial[2]. This compound reacts slowly with an excess of 1- or 1,4-substituted 1,3-dienes in methanol with cleavage of the decalin moiety to give the adducts *(4)* in *very* good yields.



(4)

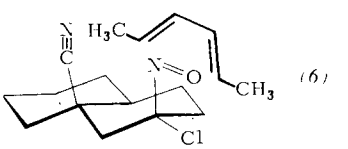
R^1	R^2
CH_3	H
CH_3	CH_3
C_6H_5	CH_3

(1) can be resolved into the antipodes *via* its methoxycarbonylhydrazone[3]; according to the sign of its Cotton effect ($\Delta\varepsilon = +1.45$ at 290.5 nm), (+)-*(1)*, $[\alpha]_{578}^{22} = +82.5°$ (ethanol, $c = 0.831$), has 9*R*,10*S* configuration. (−)-(2*S*,9*R*,10*S*)-*(3)*, $[\alpha]_{578}^{22} = -125°$ (ethanol, $c = 0.480$), obtained from (+)-*(1)* reacts (20 °C, 7d) with *trans*,*trans*-2,4-hexadiene to give optically active *(4)*, $R^1 = R^2 = CH_3$, in 83 % yield; the free base of *(4)*, b.p. 32 °C/1.5 torr, has $[\alpha]_{578}^{22} = -25.9°$ (CH_2Cl_2, $c = 0.71$).



(5)

Degradation of *(4)*, $R^1 = R^2 = CH_3$, according to the above scheme leads to a mixture of acids from which the *O*-acetyllactic acid *(5)* can be separated by chromatography on silica gel; *(5)*, b.p. 51 °C/27 torr, has $[\alpha]_{589}^{27} = -23.1°$ (acetonitrile, $c = 0.735$). This corresponds to an optical purity of 39 % and the *S*-configuration of C-6 in *(4)*.



(6)

Only a few model structures come under discussion for the transition state formed by *(3)* and the diene, because of the bulkiness and rigidity of *(3)*. The proposed structure *(6)* is most consistent with the observed preference of the 3*R*,6*S*-configuration in *(4)*. The assumed preference of the position of the NO group relative to the decalin moiety is—at least for the crystalline state—confirmed by X-ray structure analysis[2].

The optical yield of the reaction described here can, of course, be improved by variation of the structure in the diene. This type of Diels-Alder reaction ought then afford a convenient entry not only to the synthesis of optically active, hydrogenated 1,2-oxazines, but also to numerous secondary products of these compounds.

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CAS Registry numbers:
(±)-*(1)*, 2826-99-5; 60426-95-1; (±)-*(2)*, 60410-91-5; (±)-*(3)*, 60410-92-6; (−)-(2*S*,9*R*,10*S*)-*(3)*, 60426-96-2; (−)-(3*R*,6*S*)-*(4)*, $R^1 = R^2 = CH_3$, 60410-90-4; (−)-*(5)*, methyl ester, 60426-97-3; *tert*-butyl hypochlorite, 507-40-4; *trans*,*trans*-2,4-hexadiene, 5194-51-4

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[2] Result of an X-ray structure analysis by *A. Gieren* and *H.-J. Siebels*, Angew. Chem. *88*, 802 (1976); Angew. Chem. Int. Ed. Engl. *15*, 760 (1976).
[3] Resolving agent: *R. B. Woodward, T. H. Kohmann*, and *C. C. Harris*, J. Am. Chem. Soc. *63*, 120 (1941).

X-Ray Structure Analysis of *r*-9,*t*-2-Chloro-*c*-2-nitroso-*trans*-decalin-9-carbonitrile

By *Alfred Gieren* and *Hans-Jörg Siebels*[*]

Reaction of the oxime of 2-oxo-*trans*-decalin-9-carbonitrile with *tert*-butyl hypochlorite affords configuratively homogeneous 2-chloro-2-nitroso-*trans*-decalin-9-carbonitrile *(1)* as

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main product, which undergoes stereoselective Diels-Alder addition with 1,3-dienes[1]. Elucidation of the mechanism of this reaction required X-ray determination of the configuration and conformation of *(1)*.

(1)

Since *(1)* is very sensitive to light, it had to be handled with extensive exclusion of light even during measurement of the reflection intensities. Blue monoclinic crystals were obtained from solutions in *n*-hexane and petroleum ether[2]. Space group: $P2_1n$ with $a = 13.27_9$, $b = 15.08_5$, $c = 11.71_6$ Å, $\gamma = 84.85°$; $D_{exp} = 1.28\ g \cdot cm^{-3}$; $Z = 8$ (2 molecules per asymmetric unit), $D_X = 1.29\ g \cdot cm^{-3}$. With aid of an automatic single crystal diffractometer using Cu-Kα radiation (Ni filter) 4436 independent reflections were recorded in the range $0 \leq \theta \leq 70°$ (θ 2θ scan, 5-point measurement); 1404 reflections were unobserved ($I \leq 2\sigma_I$). The structure was solved by direct methods using the PHASDT program[3]. An *E* Fourier synthesis with the 300 greatest *E* values reproduced all the atoms (except H) to be expected from the constitutional formula. In the course of least-squares refinement – first with isotropic and then anisotropic temperature parameters – it could be shown by a difference Fourier synthesis, which also revealed all the H positions, that each molecule shows a second O position of the nitroso group having different population parameters. The ratio of the population parameters of the two O positions was 8:2 for one molecule and 7:3 for the other. Refinement converged at an *R* value of 5.9 %.

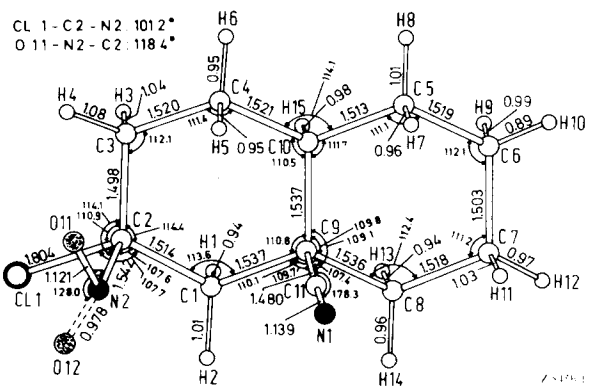

Fig. 1. Molecular structure of *r*-9,*t*-2-chloro-*c*-2-nitroso-*trans*-decalin-9-carbonitrile. The bond lengths and angles given are average values for both molecules of the asymmetric unit. The average standard deviations of the distances are 0.01 Å (except C—H: 0.03 Å; O-12—N-2: 0.02 Å), and those of the angles 0.3° (except O-12—N-2—C-2: 1°).

Figure 1 shows the molecular structure of *(1)*. The cyano group on C-9 and the nitroso group on C-2 are *cis* configurated. Steric interaction between these substituents leads to some deformation of the *trans*-decalin system: the chair shaped six-membered ring C-1 to C-9 is noticeably flattened at C-1 and C-2, as shown by the internal angles of 113.6 and 114.4° at these atoms. The NO and the C≡N groups are directed away from each other, as seen from the nonparallel bonds C-2—N-2 and C-9—C-11 in Figure 1.

The nitroso group can adopt two conformations which interconvert by rotation about C-2—N-2. In the principal oxygen site (O-11) the bonds N=O and C-2—C-3 are almost eclipsed, and in the secondary oxygen position (O-12) this applies to the bonds N=O and C-2—Cl-1. The main conformation found in the crystalline state of the nitroso group permits a steric description of the transition state of the Diels-Alder reaction of *(1)* and explains the stereoselectivity found[1].

The sp^3—sp^2 type bond C-2—N-2 is unusually long at 1.54 Å, whereas the length of the C≡N bond at 1.14 Å corresponds to expectations.

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German version: Angew. Chem. *88*, 802 (1976)

CAS Registry number:
(1), 60686-63-7

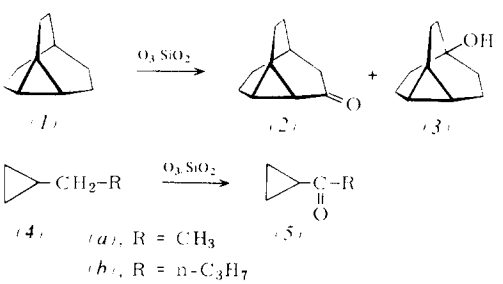
[1] *H. Nitsch* and *G. Kresze*, Angew. Chem. *88*, 801 (1976); Angew. Chem. Int. Ed. Engl. *15*, 760 (1976).
[2] We thank Professor *G. Kresze* and Dr. *H. Nitsch* for a sample of the compound.
[3] *K. Zechmeister* and *W. Hoppe*, Z. Kristallogr. *132*, 458 (1970).

Oxidation of Cyclopropyl Hydrocarbons with Ozone[**]

By *Ehrhardt Proksch* and *Armin de Meijere*[*]

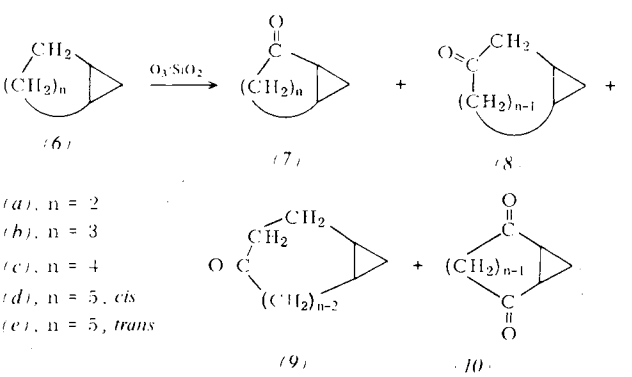
Cyclopropylcarbonyl compounds are important intermediates in preparative organic chemistry. We have found that "dry ozonization"[1] is a method for directed functionalization of cyclopropyl hydrocarbons in the α-position to the cyclopropyl group. It affords convenient entry even to those cyclopropylcarbonyl compounds for which precursors are as yet unknown or are only difficultly accessible.

In the reaction of cycloalkanes with ozone, which is adsorbed on silica gel, the tertiary positions are preferably hydroxylated[1]. Reaction of tricyclo[3.3.2.0^{2,8}]decane (hexahydrobullvalene) *(1)*, however, predominantly affords tricyclo-



[3.3.2.0^{2,8}]decan-3-one *(2)*[2] (87 % of the mixture of products) along with smaller amounts of tricyclo[3.3.2.0^{2,8}]decan-5-ol *(3)* (in 9 % yield). This preference for the secondary C—H bonds in the α-position to the cyclopropyl group is general.

Thus, the *n*-alkylcyclopropanes *(4)* yield the *n*-alkyl cyclopropyl ketones *(5)* as main products (see Table 1). The bicyclo[*n*.1.0]alkan-2-ones *(7)* are accessible in good yields from



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the bicyclo[n.1.0]alkanes *(6)*; bicyclo[n.1.0]alkan-3-ones *(9)* are formed as byproducts along with traces of the diketones *(10)*.

Exceptions are the bicyclo[2.1.0]pentane *(6)*, $n=1$, which yields, *inter alia*, cyclopropylacetic acid[9], and compound *(6e)* (see Table 1). The apparent difference in the reactions of *(6d)* and *(6e)* is consistent with the observation that energetically different carbenium ions occur as intermediates in the solvolysis of 3,5-dinitrobenzoates of the *cis*- and *trans*-bicyclo[6.1.0]nonan-2-ols[10]. Obviously, the actual radical attack of ozone at a C—H bond[11] will be determined by a polar effect[12] favoring attack at such positions at which a partial

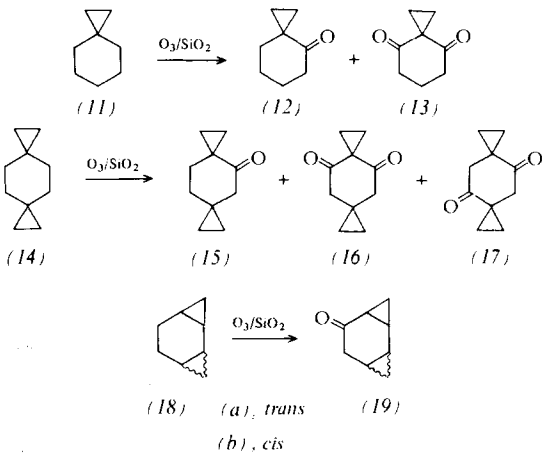

Table 1. Composition of product mixtures obtained on "dry ozonization" of cyclopropyl hydrocarbons.

Educt		Amount of product (%) [a]								Ref.
(4a)	*(4a)*	5	*(5a)*	95						[3]
(4b)	*(4b)*	5	*(5b)*	87						[4]
(6a)	*(6a)*	2	*(7a)*	93	*(8a)*	5		*(10a)*	0	[3, 5]
(6b)	*(6b)*	3	*(7b)*	95	*(8b)*	1		*(10b)*	1	[2, 3]
(6c)	*(6c)*	2	*(7c)*	85	*(8c)*	0	*(9c)* 11	*(10c)*	2	[3, 6]
(6d)	*(6d)*	3	*(7d)*	88	*(8d)*	0	*(9d)* 7	*(10d)*	2	[7]
(6e)	*(6e)*	10	*(7e)*	36	*(8e)*	10	*(9e)* 40	*(10e)*	4	[7]
(11)	*(11)*	9	*(12)*	64	*(13)*	27				[2, 3]
(14)	*(14)*	45	*(15)*	23	*(16)*	18	*(17)* 14			[2, 8]
(18a)	*(18a)*	4	*(19a)*	96						[2]
(18b)	*(18b)*	27	*(19b)*	73						[2]

[a] As a rule, 200–500 mg of the hydrocarbon was ozonized. In an experiment with 500 mg *(6b)* the yield of chromatographically isolated *(7b)* was 60 %. In other isolations using larger quantities the yields are 20–30 % higher.

positive charge can be stabilized by the cyclopropyl neighboring group. Accordingly, the selectivity of the ketonization is greater in the case of spiro[2.5]octane *(11)* than in *(6)*: α-oxidation to the spiro[2.5]octan-4-one *(12)* and the dione *(13)* takes place exclusively. The dispiro[2.2.2.2]decane *(14)* affords about equal amounts of the monoketone *(15)* and the isomeric diketones *(16)* and *(17)*.

Starting from the *trans*- and *cis*-tricyclo[5.1.0.0^{2,4}]octanes *(18a)* and *(18b)* this method affords the first entry to the tricyclo[5.1.0.0^{2,4}]octan-6-ones *(19a)* and *(19b)*, which are of importance as precursors for the *trans*-[13] and the previously unknown *cis*-tris-σ-homobenzene.

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German version: Angew. Chem. 88, 802 (1976)

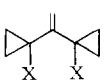
CAS Registry numbers:
(1), 283-49-8; *(2)*, 1746-95-8; *(3)*, 60582-63-0; *(4a)*, 1191-96-4; *(4b)*, 930-57-4; *(5a)*, 765-43-5; *(5b)*, 6705-46-0; *(6a)*, 285-58-5; *(6b)*, 286-08-8; *(6c)*, 286-43-1; *(6d)*, 13757-43-2; *(6e)*, 39124-79-3; *(7a)*, 4160-49-0; *(7b)*, 5771-58-4; *(7c)*, 16335-43-6; *(7d)*, 16739-31-0; *(7e)*, 16739-33-2; *(8a)*, 1755-04-0; *(8b)*, 60582-64-1; *(8e)*, 22562-45-4; *(9c)*, 49565-06-2; *(9d)*, 22562-46-5; *(9e)*, 22562-47-6; *(10b)*, 60582-65-2; *(10c)*, 37621-43-5; *(10d)*, 60582-66-3; *(10e)*, 60582-67-4; *(11)*, 185-65-9; *(12)*, 2205-98-3; *(13)*, 60582-68-5; *(14)*, 24518-94-3; *(15)*, 60582-69-6; *(16)*, 60582-70-9; *(17)*, 36262-35-8; *(18a)*, 50895-58-4; *(18b)*, 50695-42-6; *(19a)*, 60582-71-0; *(19b)*, 60619-15-0; ozone, 10028-15-6

[1] *Z. Cohen, E. Keinan, Y. Mazur*, and *T. H. Varkony*, J. Org. Chem. *40*, 2141 (1975).
[2] The structures of the new compounds were determined on the basis of their mass, IR and ^{1}H-NMR spectra. For all known compounds these spectra were in accord with published data [3–6] or with those of authentic samples.
[3] Houben-Weyl: Methoden der Organischen Chemie, 4th edit. Vol. 4/3. Thieme, Stuttgart 1971, and literature cited therein.
[4] *M. Hanack* and *H. M. Ensslin*, Justus Liebigs Ann. Chem. *697*, 100 (1966).
[5] *L. D. Hess* and *J. N. Pitts jr.*, J. Am. Chem. Soc. *89*, 1973 (1967).
[6] *A. C. Cope, S. Moon*, and *C. H. Park*, J. Am. Chem. Soc. *84*, 4848 (1962).
[7] *K. B. Wiberg* and *A. de Meijere*, Tetrahedron Lett. *1969*, 59.
[8] *T. Tsuji, S. Nishida*, and *H. Tsubomura*, J. Chem. Soc. Chem. Commun. *1972*, 284.
[9] The central C—C bond which is known to be reactive towards electrophiles is apparently attacked in this case. Investigations on the mechanism of this reaction are currently in progress.
[10] *K. B. Wiberg* and *T. Nakahira*, J. Am. Chem. Soc. *93*, 5193 (1971).
[11] *F. E. Story, D. E. Enge*, and *R. W. Murray*, J. Am. Chem. Soc. *98*, 1880 (1976).
[12] Cf. *C. Rüchardt*, Angew. Chem. *82*, 845 (1970); Angew. Chem. Int. Ed. Engl. *9*, 830 (1970).
[13] *M. Engelhardt* and *W. Lüttke*, Angew. Chem. *84*, 346 (1972); Angew. Chem. Int. Ed. Engl. *11*, 310 (1972).

Coupling Reactions of Vinylidenedicyclopropanes Doubly Halogenated in Allylic Positions—A Productive Synthesis of Trispiro[2.0.2.0.2.0]nonane ([3]Rotane)[**]

By *Lutz Fitjer*[*]

Vinylidenedicyclopropanes *(1)* which are doubly halogenated and metalated in the allylic positions were formerly unknown. They contain a tricyclopropyl synthon and as 1,3-difunctional molecules should possess considerable potential for the formation of cyclic systems. It therefore appeared particularly rewarding to examine their utility in the synthesis of the otherwise difficultly accessible [n]rotanes *(2)*, $n=3$, 4, 5...



(1), X = Halogen, Metal

(2), n = 3, 4, 5...

We now report the first synthesis of two vinylidenedicyclopropanes *(6)* and *(8)* which are doubly halogenated in their allylic positions; their intramolecular coupling to give the dispiroheptanes *(7)*[1] and *(9)* provides an entry to the entire [n]rotane series *(2)*[1, 2].

We obtained *(6)*[3] and *(8)*[3] by double ring opening of dicyclopropyl ketone *(3)*[4] with bromine in chloroform, recyclization of the resulting *meso*/(±)-1,3,5,7-tetrabromoheptan-4-one *(4)*[3] with sodium hydroxide in diethylene glycol to give 1,1'-dibromodicyclopropyl ketone *(5)*[3, 5], and subsequent methylenation and cyclopropylidenation, respectively, in the presence of potassium *tert*-butoxide.

Metalation and intramolecular coupling of *(6)* and *(8)* to form 7-methylenedispiro[2.0.2.1]heptane *(7)*[1] and 7-cyclopropylidenedispiro[2.0.2.1]heptane *(9)*[3] was accomplished

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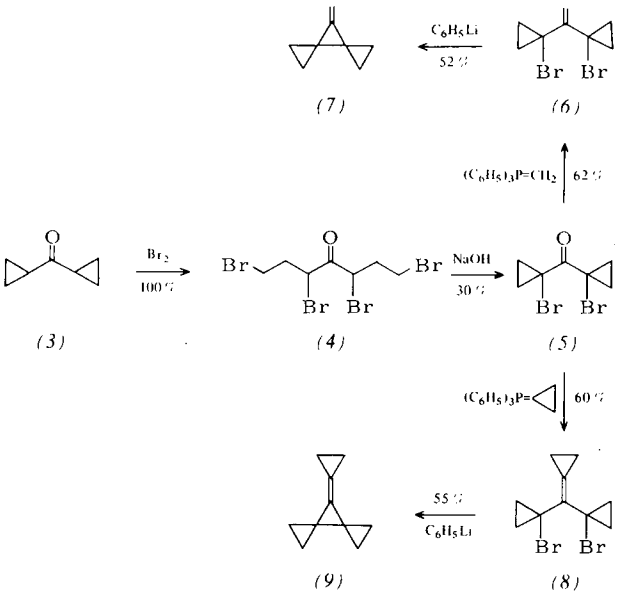
[**] This work was supported by the Deutsche Forschungsgemeinschaft.



with phenyllithium in ether. Methyl-, *n*-butyl-, and *tert*-butyllithium led to dialkylated products.

The above method of preparing *(7)* and *(9)* means that productive syntheses are available for all rotanes. While *(7)* can be transformed quantitatively into [3]rotane *(2)*, $n=3$, by cyclopropanation[6], the higher rotanes *(2)*, $n=4$, 5, 6 can all be prepared by way of *(9)*[2].

Experimental:

To prepare *(5)*, two equivalents of bromine were added dropwise to a solution of *(3)*[4] in chloroform maintained at 50 to 60°C and the compound *(4)*, obtained in crude state on removal of the solvent, was cyclized by dropping it into a suspension of three equivalents of sodium hydroxide in diethylene glycol at 40 to 50°C. Methylenation and cyclopropylidenation were accomplished by treating benzene solutions of *(5)* at 60°C portionwise with 1:1 mixtures of methyl- and cyclopropyl-triphenylphosphonium bromide, respectively, and potassium *tert*-butoxide; reactions were stopped when no ketone could be detected, even after hydrolysis. Compounds *(7)* and *(9)* were prepared by dropwise addition of ethereal solutions of *(6)* and *(8)* at 0°C to 1.1 equivalents of phenyllithium in ether.

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German version: Angew. Chem. *88*, 803 (1976)

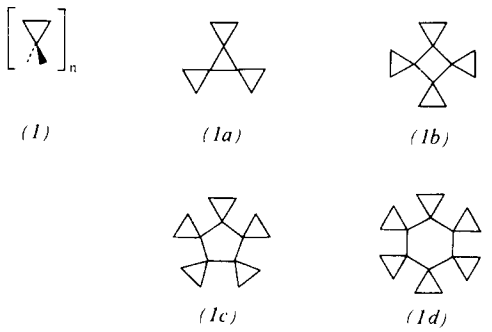
CAS Registry numbers:
(3), 1121-37-5; *meso-(4)*, 60538-58-1; (±)-*(4)*, 60538-59-2; *(5)*, 60538-60-5; *(6)*, 60538-61-6; *(7)*, 50874-25-4; *(8)*, 60538-62-7; *(9)*, 60538-43-4; methyltriphenylphosphonium bromide, 1779-49-3; cyclopropyltriphenylphosphonium bromide, 14114-05-7

[1] *L. Fitjer* and *J. M. Conia*, Angew. Chem. *85*, 832 (1973); Angew. Chem. Int. Ed. Engl. *12*, 761 (1973).
[2] *L. Fitjer*, Angew. Chem. *88*, 804 (1976); Angew. Chem. Int. Ed. Engl. *15*, 763 (1976).
[3] The new compounds *(4)* to *(6)*, *(8)*, and *(9)* gave correct elemental analyses. Their spectroscopic data are in accord with the structures given. Compound *(7)* was identical with a sample prepared according to ref. [1].
[4] *O. E. Curtis Jr.*, *J. M. Sandri*, *R. E. Crocker*, and *H. Hart*, Org. Synth. *4*, 278 (1963).
[5] Compound *(5)* is not accessible by direct bromination of dicyclopropyl ketone *(3)*. The synthetic pathway described above can be generalized: 3,5-dihalopentan-2-ones afford 1-acyl-1-halocyclopropanes (*L. Fitjer*, unpublished).
[6] Cf. ref. [1]; conversion is quantitative after 30 min on use of a fourfold excess of Simmons-Smith reagent.

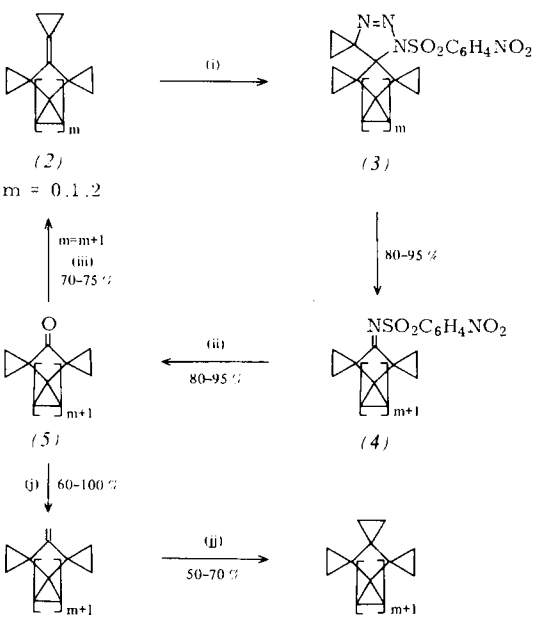
A Universal Rotane Synthesis—Hexaspiro[2.0.2.0.2.0.2.0.2.0.2.0]octadecane ([6]Rotane)[**]

By *Lutz Fitjer*[*]

Although the synthesis of the first [*n*]rotanes *(1b)* and *(1c)* was accomplished several years ago, neither the reactions nor the physicochemical properties of these hydrocarbons have yet been studied in detail. One reason is the restricted availability of the rotanes so far reported [*(1a)* to *(1c)*], which are accessible only by mutually independent total syntheses[1].



We have reported[2] a productive synthesis of [3]rotane *(1)*, $n=3$, and now present a method permitting the synthesis of each of the higher rotanes *(1)*, $n=4$, 5, 6. The main feature of this synthesis is a closed homologation sequence *(2)* → *(3)* → *(4)* → *(5)* → *(2)* which can, in principle, be repeated as often as desired. Its utility stems from the pronounced regioselectivity with which *p*-nitrobenzenesulfonyl azide (i) adds to the cyclopropylidenepolyspiroalkanes *(2)*[3]. Reaction proceeds *via* the unstable 2-triazolines *(3)* to give the ring-expanded imides *(4)*, which can be converted into the ketones *(5)* by alkaline hydrolysis (ii). At this stage a choice is possible



(i): p-$NO_2C_6H_4SO_2N_3$
(ii): KOH/CH_3OH
(iii): $(C_6H_5)_3P=$ [2]
(j): $(C_6H_5)_3P=CH_2$ [1a, 1b, 2]
(jj): CH_2I_2, Zn/Cu [1a, 1b], Zn/Ag [6]

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between methylenation (j) with subsequent cyclopropanation (jj), to give the rotanes *(1)* with $n=m+4$, or cyclopropylidenation (iii), in order to repeat the homologation sequence.

Starting from 7-cyclopropylidenedispiro[2.0.2.1]heptane *(2)*, $m=0$[2], we have not only devised a convenient preparation of the key compounds *(5)*, $m=0$ and $m=1$, for the known syntheses of [4]rotane *(1b)*[1a] and [5]rotane *(1c)*[1b], but also accomplished the first preparation of [6]rotane *(1d)* *via* *(5)*, $m=2$[5].

Since the partial structure of *(2)* responsible for the regioselectivity of the cycloaddition *(2)* → *(3)* does not change for $m>2$, the method described should permit synthesis of [*n*]rotanes with $n>6$.

[6]Rotane *(1d)* crystallizes from ether as coarse platelets (m.p. 211 to 214 °C) and is shown by its IR, ^{1}H-NMR, and ^{13}C-NMR spectra to exist in a fixed chair form at room temperature.

In order to determine the inversion barrier we have studied the temperature dependence of its ^{1}H-NMR spectrum (100 MHz, hexachlorobutadiene, *p*-dichlorobenzene as internal standard): the AA'BB' system centered at $\delta_{TMS}=0.05$ ppm with $\Delta\nu=83.3\pm0.2$ Hz, which is characteristic for *(1d)*, coalesces at 177 ± 2 °C. Insertion of these data into the Eyring relation affords $\Delta G^{\ddagger}_{450}=22.0\pm0.1$ kcal/mol, the highest inversion barrier for a cyclohexane derivative so far known.

Experimental:

The cyclopropylidenepolyspiroalkanes *(2)* are homologized by refluxing solutions of *p*-nitrobenzenesulfonyl azide in acetonitrile (saturated in the cold) with equivalent amounts of *(2)* for 12 to 16 h, hydrolyzing the imides *(4)* (which crystallize on cooling) with 5 % methanolic potassium hydroxide solution at 60 °C, and cyclopropylidenating the resulting ketones *(5)* in the manner described in ref. [2]. Compound *(1d)* is prepared by methylenating *(5)*, $m=2$, as described in ref. [2] and cyclopropanating *(6)*, $m=2$, by the procedure given in ref. [6].

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revised: September 6, 1976 [Z 552b IE]
German version: Angew. Chem. *88*, 804 (1976)

CAS Registry numbers:
(1a), 31561-59-8; *(1b)*, 24375-17-5; *(1c)*, 22748-12-5; *(1d)*, 60538-42-3; *(2)*, $m=0$, 60538-43-4; *(2)*, $m=1$, 60538-44-5; *(2)*, $m=2$, 60538-45-6; *(3)*, $m=0$, 60538-46-7; *(3)*, $m=1$, 60538-47-8; *(3)*, $m=2$, 60538-48-9; *(4)*, $m+1=1$, 60538-49-0; *(4)*, $m+1=2$, 60538-50-3; *(4)*, $m+1=3$, 60538-51-4; *(5)*, $m+1=1$, 24375-15-3; *(5)*, $m+1=2$, 22748-15-8; *(5)*, $m+1=3$, 60538-52-8; *(6)*, $m+1=1$, 24375-16-4; *(6)*, $m+1=2$, 33018-15-4; *(6)*, $m+1=3$; 60538-53-6; *p*-$NO_2C_6H_4SO_2N_3$, 938-10-3; KOH, 1310-58-3; $(C_6H_5)_3P{=}C(CH_2)_2$, 14633-95-5; $(C_6H_5)_3P{=}CH_2$, 3487-44-3; CH_3I_2, 75-11-6

[1] a) *(1b)*: *J. M. Conia* and *J. M. Denis*, Tetrahedron Lett. *1969*, 3545; *P. LePerchec* and *J. M. Conia*, *ibid.* *1970*, 1587; b) *(1c)*: *J. L. Ripoll* and *J. M. Conia*, *ibid.* *1969*, 979; *J. L. Ripoll*, *J. C. Limasset*, and *J. M. Conia*, Tetrahedron *27*, 2431 (1971); c) *(1a)*: *L. Fitjer* and *J. M. Conia*, Angew. Chem. *85*, 349, 832 (1973); Angew. Chem. Int. Ed. Engl. *12*, 334, 761 (1973).

[2] *L. Fitjer*, Angew. Chem. *88*, 803 (1976); Angew. Chem. Int. Ed. Engl. *15*, 762 (1976).

[3] Regioselective cycloadditions of azides to alkylidenecycloalkanes are known and have been employed for ring expansion [4]; the only cycloalkylidenecycloalkane examined so far, cyclopropylidenecyclohexane, however, does not add cyanogen azide regioselectively and leads to a mixture of ring-expanded imides [4a].

[4] a) *J. E. McMurry* and *A. P. Coppolino*, J. Org. Chem. *38*, 2821 (1973); b) *R. A. Wohl*, *ibid.* *38*, 3862 (1973).

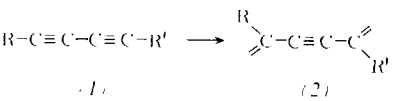
[5] The new compounds *(1d)*, *(2)*, $m=1, 2$, *(4)*, $m=0, 1, 2$, *(5)*, $m=2$, and *(6)*, $m=2$ gave correct analytical values. Their IR and ^{1}H-NMR spectra are in accord with the structures given. The composition of *(1d)* was also confirmed by mass spectrometry.

[6] *J. M. Denis*, *C. Girard*, and *J. M. Conia*, Synthesis *1972*, 549.

Polymerization of Tricosa-10,12-diynoic Acid in Multilayers

By *B. Tieke*, *G. Wegner*, *D. Naegele*, and *H. Ringsdorf*[*]

Oriented layers constructed from monomolecular films by means of the Langmuir-Blodgett (LB) technique have achieved great significance in physicochemical studies. However, most are unstable, and ultimately break apart in order to reorganize in the form of microcrystals. Hence, attempts have not been lacking to construct such layers from long-chain vinyl derivatives and to polymerize these with retention of the layer structure[1]. More suitable for this purpose ought to be the topochemical polymerization of diacetylenes, which leads with retention of the molecular packing in the crystal lattice to chains containing conjugated double and triple bonds[2]. The fact that the single crystals of polydiacetylenes studied so far have proven themselves as one-dimensional semiconductors[3] aroused additional interest in the construction of extended multilayers of these polymers.



(1) *(2)*

R = $-(CH_2)_9-CH_3$
R' = $-(CH_2)_8-CO_2H$

Using the LB technique[4] we have prepared multilayers on quartz supports of the Cd salt of tricosa-10,12-diynoic acid *(1)* from monomolecular films. They were characterized by their UV spectra and by measurement of the (001) reflections in the X-ray diffractometer. The long spacing (5 orders) was found to be 51.5 Å. Since the length of the molecule as estimated from known bond lengths and angles amounts to *ca.* 30 Å, the molecules must be oriented head-to-head-to-tail-to-tail in the layers, *i.e.* Y layers must be present. The angle of the longest molecular axis to the surface of the support is then *ca.* 60°. The absorption bands of the conjugated triple bonds appear at $\lambda=217$, 230, 242, and 256 nm.

The multilayer was polymerized by irradiation at 254 nm. The UV spectrum obtained after 20 min corresponds to that of the pure polymer *(2)*. Maxima are observed at 537 nm

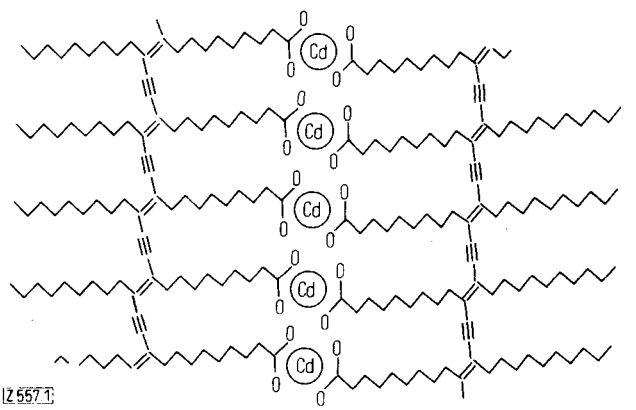


Fig. 1. Structure of a layer after polymerization.

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($\varepsilon = 1.5 \times 10^4$ cm^{-1}) and 498 nm ($\varepsilon = 1.63 \times 10^4$ cm^{-1}). The X-ray data show that the arrangement of the layers remains unaltered. The polymer layers (Fig. 1 shows their structure) are stable at room temperature under normal laboratory conditions (O_2, light, *etc.*) and show no signs of reorganization even after several months.

Synthesis of (1)[5]:

Undecynoic acid (0.02 mol) is neutralized with 10% KOH (15 ml). To this solution are added successively hydroxylamine hydrochloride (100 mg) and copper(I) chloride (500 mg) in 70% aqueous ethylamine (4 g). A solution of 1-iodo-1-dodecyne (0.02 mol) in methanol (10 ml) is then added dropwise with vigorous stirring to the cold reaction mixture. After acidification with 2 N H_2SO_4 the mixture is extracted with ether, the etheral phase dried over sodium sulfate, and the ether removed by distillation. The residue is treated with petroleum ether (b.p. 40—60°C), from which *(1)* crystallizes on cooling. Yield: 3.5 g (45.5%); m.p. 56.5°C.

Preparation of multilayers of (1):

(1) was sprayed onto an aqueous 2×10^{-4} M solution of $CdCl_2$ in a Langmuir trough. The monomolecular films that were formed were successively transferred by the LB technique onto ultra-pure quartz platlets until a multilayer of defined thickness was obtained.

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CAS Registry numbers:
(1), 60705-19-3; *(2)*, 60705-85-3; undecynoic acid, 2717-65-3; 1-iodo-1-dodecyne, 60705-20-6

[1] *M. Puterman, T. Fort jr.*, and *J. B. Lando*, J. Colloid Interface Sci. *47*, 705 (1974); *R. Ackermann, D. Naegele*, and *H. Ringsdorf*, Makromol. Chem. *175*, 699 (1974).
[2] *G. Wegner*, Makromol. Chem. *154*, 35 (1972); Chimia *28*, 475 (1975).
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[4] *K. B. Blodgett*, J. Am. Chem. Soc. *57*, 1007 (1935); *H. Kuhn, D. Möbius*, and *H. Bücher* in *A. Weissberger* and *B. Rossiter*: Techniques of Chemistry, Wiley, New York 1972, Vol. I, Part IIIb, Chap. VII; *H. Kuhn* and *D. Möbius*, Angew. Chem. *83*, 672 (1971); Angew. Chem. Int. Ed. Engl. *10*, 620 (1971).
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S_4N_4 Bridge Ligand: Structure of $CuCl \cdot S_4N_4$[**]

By *Ulf Thewalt*[*]

Addition compounds of S_4N_4 and Lewis acids are well known[1]. In the X-ray spectrographically investigated compounds $SbCl_5 \cdot S_4N_4$[2] and $BF_3 \cdot S_4N_4$[3], S_4N_4 functions as monodentate ligand, which is bound *via* a N atom to the central atom of the Lewis acid. Both compounds contain discrete $MX_n \cdot S_4N_4$ structural units.

Since the empirical formulas of the novel compounds $CuCl \cdot S_4N_4$, $CuBr \cdot S_4N_4$, and $CuCl_2 \cdot S_4N_4$ afford no clue to the actual structure of the complexes an X-ray structure analysis[4] was carried out on $CuCl \cdot S_4N_4$ *(1)*. Compound *(1)* is slowly formed on allowing a solution of S_4N_4 and $CuCl_2 \cdot 2H_2O$ in benzene/ethanol to stand for several hours. The well-formed, lustrous, anthracite-black crystals are stable towards air and water, do not dissolve in any of the common solvents, and decompose without melting on being heated.

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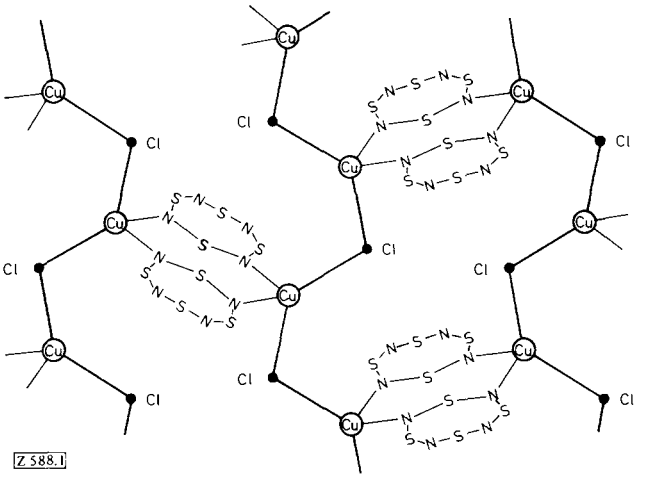

Fig. 1. Structure of a $[CuCl \cdot S_4N_4]_x$ layer (schematic).

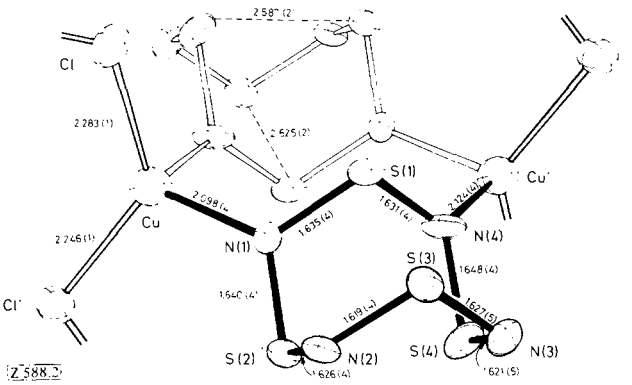

Fig. 2. Section from the crystal structure of $CuCl \cdot S_4N_4$ *(1)* with bond lengths in Å. The internal angles in the S_4N_4 unit are: S(1) 103.6(2)°, S(2) 104.4(2)°, S(3) 104.8(2)°, S(4) 103.9(2)°, N(1) 112.8(2)°, N(2) 113.6(2)°, N(3) 113.7(2)°, N(4) 112.6(2)°; other bond angles: Cl—Cu—Cl' 129.1(1)°, N(1)—Cu—N(4') 103.9(2)°, Cu—Cl—Cu'' 110.0(1)°, S(1)—N(1)—Cu 120.6(2)°, S(2)—N(1)—Cu 125.3(2)°, S(1)—N(4)—Cu' 126.9(2)°, S(4)—N(4)—Cu' 119.9(2)°.

In the crystal, zig-zag chains $[Cu—Cl]_x$ are present and all are oriented parallel to the *z* axis (long axis of the crystal, cf. Fig. 1). Cu atoms of neighboring chains are each bridged by two S_4N_4 rings. The resulting layers and neighboring layers of the same type are held together by Van der Waals forces. As in $SbCl_5 \cdot S_4N_4$ and $BF_3 \cdot S_4N_4$, the S_4N_4 moiety in *(1)* is bound *via* nitrogen to the metal atom; however, in *(1)* a S_4N_4 ring is bound by two coordinate bonds. The Cu atom is tetrahedrally coordinated. Surprisingly, the S_4N_4 group in *(1)* differs only slightly in its dimensions and not at all in its conformation from free S_4N_4[6]; the N atoms lie at the corners of a square (exactly in one plane), the S atoms are situated alternately above and below this square, and there are two short transannular S···S distances. In comparison, the S_4N_4 group in the complexes $SbCl_5 \cdot S_4N_4$ and $BF_3 \cdot S_4N_4$ has an inverse conformation, *i.e.* with the S atoms occupying the corners of a square[2, 3].

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CAS Registry numbers:
(1), 60788-82-1

[1] *J. Weiss*, Fortschr. Chem. Forsch. *5*, 635 (1966); *K. J. Wynne* and *W. L. Jolly*, Inorg. Chem. *6*, 107 (1967).
[2] *D. Neubauer* and *J. Weiss*, Z. Anorg. Allg. Chem. *303*, 28 (1960).
[3] *M. G. B. Drew, D. H. Templeton*, and *A. Zalkin*, Inorg. Chem. *6*, 1906 (1967).
[4] Crystal data: monoclinic prismatic *c*; space group $P2_1/c$; $a = 9.053(2)$, $b = 11.755(4)$, $c = 6.749(2)$ Å, $\beta = 104.48(2)°$; $Z = 4$; $d_{x\text{-ray}} = 2.705$, $d_{exp} = 2.71$ g·cm^{-3}. Structure determination and refinement based on 1636 indepen-

dent reflections for $\theta = 28°$ measured on a Siemens AED instrument with Mo-K_α radiation; $R = 0.057$, $R_w = 0.059$. Programs by *Sheldrick* [5] where used for the calculations.

[5] *G. M. Sheldrick*, Cambridge, unpublished.

[6] Bond lengths and angles in free S_4N_4[7] ⟨S—N⟩ = 1.616 Å, S···S = 2.58 and 2.59 Å; ⟨SNS⟩ = 113°, ⟨NSN⟩ = 105°.

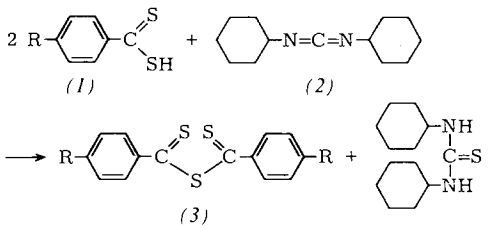
[7] *B. D. Sharma* and *J. Donohue*, Acta Cryst. *16*, 891 (1963).

Isolation of Crystalline Bis(thioacyl) Sulfides

By *Shinzi Kato*, *Tomonori Katada*, and *Masateru Mizuta*[*]

While carboxylic anhydrides are well known, their sulfur analogs *(3)* have remained unknown so far because of their instability[1].

We now report the isolation of the first bis(thioaroyl) sulfides *(3)*. The compounds listed in Table 1 are obtained on reaction of aromatic dithiocarboxylic acids *(1)* with dicyclohexylcarbodiimide *(2)* at 0°C. The crystalline thioanhydrides *(3a)* and *(3b)* are fairly stable in the solid state at room temperature in the dark, but the oily compounds *(3c)* and *(3d)* decompose completely within 1 h under similar conditions.



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

Table 1. Bis(thioaroyl) sulfides *(3)* synthesized.

	R	Yield [%]	M.p. [°C]	UV (cyclohexane) λ_{max}	(ε_{max})	IR (KBr) $\nu_{as}C{=}S$ [cm^{-1}]
(3a)	CH_3	80	74—75	334 nm (25000)	568 nm (150)	1232, 1242
(3b)	CH_3O	85	65—66	355 nm (35900)	559 nm (365)	1245, 1270
(3c)	H	75	oil	307 nm (14600)	548 nm (145)	1245 [a]
(3d)	Cl	78	oil	323 nm (16800)	548 nm (155)	1245 [a]

[a] Neat.

The structures proposed for *(3a)* to *(3d)* are in accord with the results of elemental analysis and UV, IR, and ^{1}H-NMR spectroscopic data. The UV absorption at 310 to 350 nm is due to the $\pi \rightarrow \pi^*$ transition, and that at 550 to 570 to the $n \rightarrow \pi^*$ transition of the thiocarbonyl groups.

Experimental:

Freshly prepared 4-methyldithiobenzoic acid *(1a)* (3.36 g, 0.02 mol) and *N,N'*-dicyclohexylcarbodiimide *(2)* (2.06 g, 0.01 mol) are stirred in *n*-hexane (80 ml) under nitrogen for 1 h at 0°C. Removal of the precipitate (*N,N'*-dicyclohexylthiourea, 2.28 g) by filtration, evaporation of the solvent, and recrystallization of the resulting residue from petroleum ether (b. p. < 40°C) gives dark green needle crystals of bis(4-methylthiobenzoyl)sulfide *(3a)* (2.46 g, 80%).—NMR (CCl_4): δ [ppm]: 2.32 (s, 6H, CH_3), 7.05 (*ca.* d, 4H), 7.82 (*ca.* d, 4H).

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CAS Registry numbers:
(1a), 2168-80-1; *(1b)*, 2168-77-6; *(1c)*, 121-68-6; *(1d)*, 2168-82-3; *(2)*, 538-75-0; *(3a)*, 60410-77-7; *(3b)*, 60410-78-8; *(3c)*, 22778-02-5; *(3d)*, 60410-79-9

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Department of Chemistry, Faculty of Engineering, Gifu University
Kagamihara, Gifu 504 (Japan)

[+] To whom correspondence should be addressed.

[1] Thioanhydrides of dithiocarbamic acid [$(R_2NCS)_2$S] and xanthic acid [$(ROCS)_2$S] have been reported: *D. H. Powers*, U. S. Patent 1788632 (Jan. 1930); Chem. Abstr. *25*, 4890 (1931); *A. Gutmann*, Ber. Dtsch. Chem. Ges. *56*, 2365 (1923); *S. N. Danilov* and *N. M. Grad*, Zh. Obshch. Khim. *17*, 2193 (1947); Chem. Abstr. *43*, 1181 (1949); *S. V. Zhuravlev* and *M. I. Galchenko*, Zh. Prikl. Khim. *20*, 1038 (1947); Chem. Abstr. *43*, 143 (1949); *J. Wortmann* and *G. Gattow*, Z. Anorg. Allg. Chem. *377*, 79 (1970); *M. Muraoka*, *T. Yamamoto*, and *T. Takeshima*, Bull. Chem. Soc. Jpn. *48*, 2462 (1975).

Arsenic Oxide Trichloride, $AsOCl_3$[**]

By *Konrad Seppelt*[*]

Like arsenic pentachloride, which remained undiscovered for some 140 years, existence of the oxide chloride of arsenic, $AsOCl_3$ has so far not been reported. On the other hand $POCl_3$ has been known since 1847 and is presently produced on an industrial scale.

Two problems were expected to beset the preparation of $AsOCl_3$: a) decomposition with evolution of chlorine and reduction to trivalent arsenic, and b) the tendency of the As=O double bond to polymerization, for $AsOF_3$ is known only in the polymeric form[1]. Attempts to prepare $AsOCl_3$ by careful hydrolysis of $AsCl_5$[2] met without success because the HCl formed catalyzed the decomposition of $AsCl_5$. However, $AsOCl_3$ can be prepared surprisingly simply by ozonization of $AsCl_3$ in inert solvents at low temperatures.

The reaction proceeds quantitatively and results in precipitation of $AsOCl_3$. Its structure is proved by the mass spectrum [m/e = 196 ($AsOCl_3^+$, 42%), 180 ($AsCl_3^+$, 50%), 161 ($AsOCl_2^+$, 100%), and other fragments], the Raman and IR spectrum (987 cm p, 441 dp, 412 p, 256 dp, 201 p, 160 dp) and by stoichiometric take-up of ozone.

$$AsCl_5 \xrightarrow{H_2O/HCl} AsCl_3 + Cl_2$$

$$AsCl_3 + O_3 \xrightarrow[-78\,°C]{CFCl_3/CH_2Cl_2} AsOCl_3 + O_2$$

Arsenic oxide trichloride is a colorless, crystalline solid, which is considerably more thermally stable than arsenic pentachloride. As expected $AsOCl_3$ has a pyramidal structure, the oxygen atom being double bonded. This is confirmed by the Raman spectrum, which closely resembles that of $AsCl_3$ with regard to some of the bands. A calculation of force constants[3] gives a value of $f = 7.47$ mdyne/Å for the arsenic-oxygen bond, *i. e.* $AsOCl_3$ is one of the few compounds containing a real arsenic-oxygen double bond. The calculation also

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shows that the strength of the arsenic-chlorine bond increases [2.04→2.59 mdyne/Å] in the transition $AsCl_3 \rightarrow AsOCl_3$, exactly as in the system $PCl_3 \rightarrow POCl_3$ [2.34→2.98 mdyne/Å]. The compounds are therefore also related in the details of their bonding.

$AsOCl_3$ slowly decomposes at −25 °C, and much more rapidly at *ca.* 0 °C, with formation of $As_2O_3Cl_4$.

$$3\ AsOCl_3 \longrightarrow AsCl_3 + Cl_2 + As_2O_3Cl_4$$

This compound is stable up to 150 °C. Its vibrational spectrum reveals disappearance of the As=O double bond, thus ruling out the structure $P_2O_3Cl_4[Cl_2P(O)—O—(O)PCl_2]$. It is also not volatile, but decomposes above 200 °C with loss of $AsCl_3+Cl_2$ to give "As_2O_5"—a process which can be readily monitored in the mass spectrum.

$As_2O_3Cl_4$ is obviously a polymer. It can be isolated in analytically pure form, but is X-ray amorphous. No crystallization takes place even after 50 hours' annealing at 120 °C. In this compounds arsenic is doubtless pentacoordinated, or hexacoordinated by way of chlorine bridges.

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CAS Registry numbers:
$AsOCl_3$, 60646-36-8; $AsCl_3$, 7784-34-1; O_3, 10028-15-6; $As_2O_3Cl_4$, 60646-37-9

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Bis(η-1,5-cyclooctadiene)cobaltlithium

By *Klaus Jonas, Richard Mynott, Carl Krüger, Janine C. Sekutowski*, and *Yi-Hung Tsay*[*]

Nickel(0)-olefin complexes which do not contain pronounced acceptors as ligands form defined dilithium-nickel-olefin complexes with lithium[1]. We now wish to report a further example of this class of compounds.

Reaction of metallocene complexes $(C_5H_5)_2M$ with an alkali metal leads to release of the two C_5H_5 rings and formation of alkali metal-C_5H_5 and elemental transition metal[2]. In the case of cobaltocene and nickelocene we have now found that the deposition of transition metal is suppressed on addition of cyclooctadiene (COD). The new cobalt complex *(3)* and the known nickel complexes *(1)*[3] and *(2)*[1] can then be isolated in high yield [*e.g. (3)*: 85 %][7].

$$(C_5H_5)_2Co \xrightarrow[THF,\ 0\,°C]{Li,\ COD} C_5H_5CoCOD + LiC_5H_5$$

$$C_5H_5CoCOD \xrightarrow[THF,\ 0\,°C]{2\ Li,\ COD} (COD)_2CoLi(THF)_x\ (3) + LiC_5H_5$$

$$(C_5H_5)_2Ni \xrightarrow[THF,\ 0\,°C]{2\ Li,\ 2\ COD} (COD)_2Ni + 2\ LiC_5H_5$$

$$(COD)_2Ni \xrightarrow[THF,\ 0\,°C]{2\ Li} (COD)_2NiLi_2(THF)_4\ (2)$$

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[**] ^{13}C-NMR spectra.
[***] X-Ray structure analysis.
[****] *J. C. S.* thanks the Deutsche Forschungsgemeinschaft for a study grant.

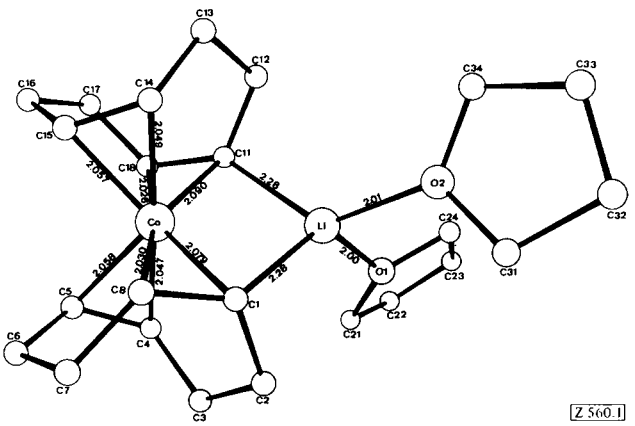
Recrystallization of *(3)* from ether gives

$(COD)_2CoLi(THF)_2$ *(3a)*

and on addition of dimethoxyethane (DME), yellow crystals of

$(COD)_2CoLi(DME)_3$ *(3b)*

are obtained. The new cobalt complexes *(3)* were characterized by metal analyses and by their reaction with CO, in which four CO per LiCo were consumed with displacement of COD. The IR spectrum (THF) shows all four double bonds are complexed both in *(3)* and in the isoelectronic compound *(1)*. The ^1H-NMR spectrum ([D_8]THF, RT) of *(3b)* displays two broad signals at $\tau = 7.57$ (—CH_2) and $\tau = 7.9$ (CH=CH), intensity ratio 2:1, for the cyclooctadiene.



Z 560.1

Fig. 1. Crystal structure of $(COD)_2CoLi(THF)_2$ *(3a)*.

Figure 1 shows the result of an X-ray structure analysis of *(3a)* [$a = 14.094(1)$, $b = 18.799(3)$, $c = 17.500(3)$ Å, $\beta = 97.74(1)°$, space group C2/c, 3219 reflections, 1485 unobserved, $R = 0.064$]. The bond angles at the cobalt atoms diverge pairwise so markedly from an ideal tetrahedron (such as occurs in the isoelectronic complex $Ni(COD)_2$[4]) that the molecule is better described as a trigonal bipyramid. Its equatorial positions are occupied by Li and by one double bond each of the two olefinic ligands [C1—C8: 1.413(7) Å; C11—C18: 1.419(7) Å]. Owing to bridging with the axial positions of the Co [C4—C5: 1.391(8) Å; C14—C15: 1.401(8) Å] the COD ligands assume a highly distorted boat conformation. Short Li—C distances (Li—C1; Li—C11) indicate strong ion-pair interaction[5] between the Li atom in a tetrahedral environment and C atoms of the double bonds in equatorial positions. The Li—Co distance [2.654(8) Å] is significantly longer than the sum of the respective covalent radii.

The ^{13}C-NMR spectrum[6] of *(3a)* at room temperature shows only two signals for the COD at 69.1 and 34.7 ppm ([D_8]THF) or at 69.5 and 33.7 ppm ([D_8]toluene). On cooling a solution in [D_8]THF the COD signals become much broader only below −60 °C. In [D_8]toluene, on the other hand, broadening begins at 0 °C, and at −77 °C eight signals of approximately equal intensity are observed. Four of the signals lie at 79.6, 74.3, 71.5, and 50.7 ppm (all d, average chemical shift 69.0 ppm), and the other four at 38.3, 38.0, 30.2, and 29.0 ppm (all t, average chemical shift 33.9 ppm). These temperature effects are reversible. The ^{13}C-NMR spectrum of *(3a)* in [D_8]toluene at −77 °C is compatible with the structure of the crystalline complex: owing to the equatorial position of the Li atom on the cobalt, four distinct pairs of olefinic and aliphatic C atoms are expected. On raising the temperature in [D_8]toluene, the Li atom is found to undergo a shift in

the $(COD)_2Co$ group. The strongly solvating $[D_8]$THF accelerates this exchange.

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$(COD)_2CoLi(THF)_2$, 60718-95-8; $(C_5H_5)_2Co$, 1277-43-6; ^{13}C, 14762-74-4

[1] *K. Jonas*, Angew. Chem. *87*, 809 (1975); Angew. Chem. Int. Ed. Engl. *14*, 752 (1975); *K. R. Pörschke*, Dissertation, Universität Bochum 1975.
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[4] *H. Dierks* and *H. Dietrich*, Z. Kristallogr., Kristallgeom., Kristallphys., Kristallchem. *122*, 1 (1965).
[5] *D. J. Brauer*, *C. Krüger*, *P. J. Roberts*, and *Y.-H. Tsay*, Angew. Chem. *88*, 52 (1976); Angew. Chem. Int. Ed. Engl. *15*, 48 (1976); *R. Zerger*, *W. Rhine*, and *G. Stucky*, J. Am. Chem. Soc. *96*, 6048 (1974).
[6] The ^{13}C-NMR spectra were recorded at 25.2 MHz. Chemical shifts relative to TMS, multiplicities characterized by off-resonance procedure as d = doublet and t = triplet.
[7] We have also prepared isoelectronic complexes of iron by the same method, and are investigating further compounds of this type formed by other transition metals.

Bis(diorganylphosphinodithioformato-*S*,*P*)nickel(II) Complexes—Novel Four-Membered Ring Chelates[**]

By *Jürgen Kopf*, *Rudolf Lenck*, *Sigurjon N. Olafsson*, and *Reinhard Kramolowsky*[*]

Substituted dithioformate ions of type *(1)* react with many elements to give well known[1] four-membered ring chelates in which they coordinate *via* the two S atoms. A chelate formation with the donor atom of the residue Y and an S atom has been discussed but not proven[2].

(1) Y = NR_2, OR, SR

As novel ligands of type *(1)*, we prepared the phosphinodithioformates *(2)* by reaction of secondary phosphanes and carbon disulfide in the presence of aqueous potassium hydroxide[3,4].

$$R_2PH + CS_2 + KOH \rightarrow R_2PCS_2^-K^+ + H_2O$$

(2)

(a): R = C_6H_5[4]
(b): R = cyclo-C_6H_{11}
(c): R = $C_6H_5CH_2$

The salts *(2)* react with nickel(II) salts to give apolar, diamagnetic bis(chelates) *(3)* having the composition $[Ni(S_2CPR_2)_2]$[4,5]. We have now found that the anions of *(2)* occur as P,S-bonded chelates in these complexes, for, in contrast to *(2)*, they do not react in organic solvents at room temperature with sulfur[6]. The high-frequency position of a band attributable to an approximate C=S stretching vibration in the IR spectra (cf. Table 1) also provides evidence for this structure.

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[**] We thank Professor *Weiss* and the Deutsche Forschungsgemeinschaft for supplying the diffractometer.

Table 1. Physical properties of complexes *(3)*.

	Color	M.p. (dec.) [°C]	IR (KBr) νC=S [cm^{-1}]
(3a)	orange	198—202 [a]	1100 vs. br
(3b)	red	206—209 [b]	1087 vs. br
(3c)	rust red	153—156 [c]	1092 vs. br

[a] Dissolved in dibromomethane and precipitated with ether.
[b] From benzene.
[c] From dibromomethane/acetone.

Proof of the structure was afforded by an X-ray structure analysis of *(3b)*, which on the basis of 2121 significant reflections was solved by usual methods and refined to an *R* value 0.072. *(3b)* crystallizes in the triclinic space group $P\bar{1}$ with $a = 1073.9$, $b = 1124.5$, $c = 1448.3$ pm; $\alpha = 90.58$, $\beta = 91.12$, $\gamma = 116.94°$; $Z = 2$. The nickel atom forms an inversion center and is bonded in a planar array to two *trans* P and S atoms (see Fig. 1).

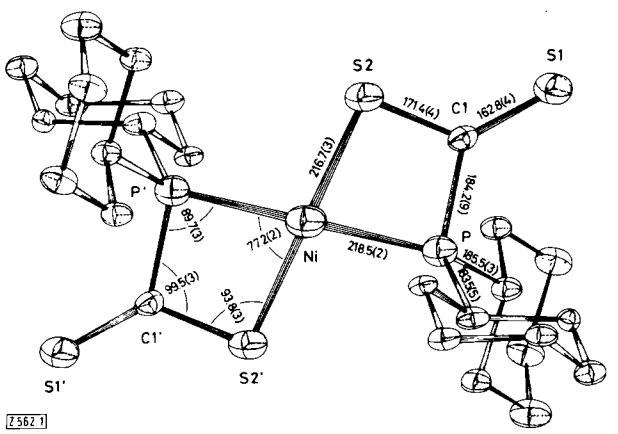
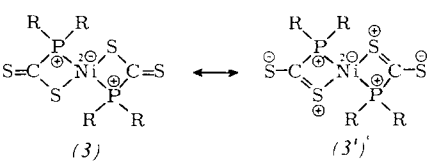


Fig. 1. Molecular structure of the bis(chelate) *(3b)* with important bond lengths (righthand side) and important bond angles (lefthand side); standard deviations in parentheses.

The exocyclic C—S bond is significantly longer than in thioformaldehyde ($r_{C=S} = 161.1$ pm)[7], and the endocyclic C—S distance is shorter than the value ($r_{C-S} = 176$ to 178 pm)[8] calculated for $C(sp^2)$—S single bonds. Together, these findings are consistent with a marked contribution of the resonance structure *(3')*. The Ni—S and Ni—P bond lengths are notably



(3) *(3')*

shorter than in all previously investigated four-membered ring chelates containing a NiS_4 skeleton ($r_{Ni-S} = 218$ to 224 pm)[1b] or planar nickel(II) complexes with *trans*-NiP_2X_2 coordination ($r_{Ni-P} = 225$ to 238 pm; X = Cl, Br)[9].

Experimental

Potassium diorganylphosphinodithioformates *(2)*: All operations must be carried out under nitrogen. A solution of the secondary phosphane (30 mmol) and carbon disulfide (30 mmol) in tetrahydrofuran (25 ml) is treated with a saturated aqueous solution of potassium hydroxide and the mixture stirred vigorously for 15 h at room temperature. After concentration of the THF solution and addition of ether [or of *n*-hexane in the case of *(2c)*] *(2)* separates out as fine, bright-pink to red crystals. Yield 80 to 85 %.

Bis(diorganylphosphinodithioformato-*S,P*)nickel(II) complex *(3)*: A solution of *(2)* (10 mmol) [in the case of *(2a)* in acetone and ether (25 ml of each), in the case of *(2b)* in acetone (25 ml), and in the case of *(2c)* in THF (20 ml) and ether (75 ml)] prepared under nitrogen is added dropwise to a solution of $Ni(NO_3)_2(H_2O)_6$ (5 mmol) in acetone (50 ml) [in the case of *(2a)* in acetone and ether (50 ml of each)]. The finely crystalline precipitate of complex *(3)* is filtered off, washed thoroughly with water and acetone, and recrystallized as quoted in Table 1. Yield 75 to 85 %.

All compounds *(2)* and *(3)* gave correct analyses[10].

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German version: Angew. Chem. 88, 811 (1976)

[1] a) *D. Coucouvanis*, Progr. Inorg. Chem. *11*, 233 (1970); b) *R. Eisenberg*, Progr. Inorg. Chem. *12*, 295 (1970).

[2] *L. Cambi* and *A. Cagnasso*, Atti Accad. Naz. Lincei *13*, 809 (1931). *B. J. McCormic*, *R. I. Kaplan*, and *B. P. Stormer*, Can. J. Chem. *49*, 699 (1971), suppose that the compounds prepared by them from aziridinenickel complexes and CS_2 contain N,S coordinated dithiocarbamates, without offering definite proof that this is so.

[3] *R. Lenck*, Diplomarbeit, Universität Hamburg 1968. The use of triethylamine or potassium phenolate instead of potassium hydroxide is described by *O. Dahl*, *N. C. Gelting*, and *O. Larsen*, Acta Chem. Scand. *23*, 3369 (1969).

[4] *R. Kramolowsky*, Angew. Chem. *81*, 182 (1969); Angew. Chem. Int. Ed. Engl. *8*, 202 (1969).

[5] Under the conditions quoted the reaction of diethylphosphane and CS_2 with nickel(II) salts described by *L. Malatesta*, Gazz. Chim. Ital. *77*, 518 (1947) does not afford the postulated complex *(3)*, R = Et, but a mixture, from which bis(diethylthiophosphinyldithioformato)nickel(II) has so far been isolated: *R. Kramolowsky* and *R. Lenck*, unpublished work.

[6] *(3b)* and *(3c)* do not react with S_8 even in boiling toluene or CH_2Br_2; *(3a)* decomposes on standing or warming, with or without S_8 in organic solvents.

[7] *D. R. Johnson*, *F. X. Powell*, and *W. H. Kirchhoff*, J. Mol. Spectrosc. *39*, 136 (1971).

[8] *G. F. Gasparri*, *M. Nardelli*, and *A. Villa*, Acta Crystallogr. *23*, 384 (1967).

[9] *P. L. Belton*, *V. Albano*, *V. D. Bianco*, *F. Pompa*, and *V. Scatturin*, Ric. Sci. *33*, 1213 (1963); *W. S. Sheldrick* and *O. Stelzer*, J. Chem. Soc. Dalton Trans. *1973*, 926.

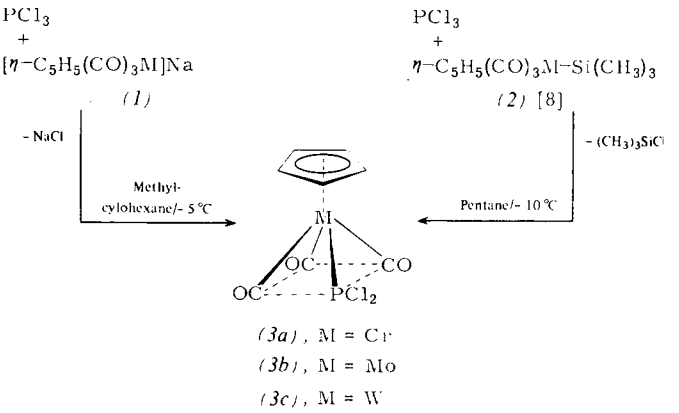
[10] Note added in proof (29. 11. 76): *(3b)* has in the meantime also been synthesized by *F. G. Moers*, *D. H. W. Thewissen*, and *J. J. Steggerda*, University of Nijmegen, using $NiCl_2(H_2O)_6$, dicyclohexylphosphane and CS_2 in the presence of triethylamine. *F. G. Moers*, personal communication.

Functional Transition-Metal Phosphanes[1]

By *Wolfgang Malisch* and *Robert Alsmann*[*]

Transition metal-substituted phosphanes have a strong tendency to undergo agglomeration with ligand elimination[2]. Only in a few sterically or electronically favorable cases are they preparatively accessible[3]. We have now been able to prepare the first functional representatives *(3)* of this class of compounds, which are obtained as air-sensitive, deeply colored crystals by metalation of phosphorus trichloride with salts of type *(1)*, or with trimethylsilyl complexes *(2)* derived therefrom.

Compounds *(3a)*—*(3c)* are only moderately soluble in pentane and cyclohexane; they are much more readily soluble in benzene or THF, but rapidly decompose with formation of the complex metal halides *(4)*. Decomposition increases in the series *(3a)* ≪ *(3c)* < *(3b)* and can be thermally accelerated[4]. The complex metal halide is accompanied by



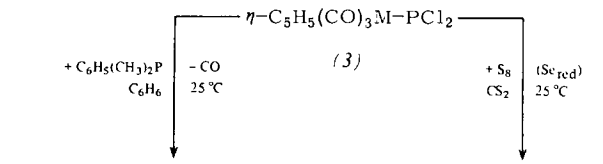
(3a), M = Cr
(3b), M = Mo
(3c), M = W

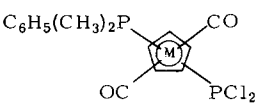
a P- and Cl-containing product which we formulate, for stoichiometric reasons, as $(PCl)_x$.

$$\underset{(3)}{\eta\text{-}C_5H_5(CO)_3M\text{—}PCl_2} \rightarrow \underset{(4)}{\eta\text{-}C_5H_5(CO)_3MCl} + (PCl)_x$$

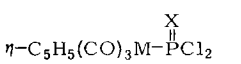
Therefore satisfactory yields (60 to 70 %) of *(3)* are only achieved in apolar solvents, especially if—starting from *(2)*—homogeneous reaction ensures a minimal stress.

The decomposition *(3)* → *(4)* affords evidence for compounds *(3)* being transition-metal analogs of alkali metal-chlorophosphanes, postulated in the reaction of polychlorinated phosphorus(III) compounds with alkali metals[5]. They are more stable, however, and should, as related systems[4] be suitable for the generation of phosphorus(I) units[6]. We presume that weakening of the central bond is the initial step of the decomposition and that a high charge density on the transition metal and phosphorus serves as the driving force for the decomposition. Consistent with this hypothesis, replacement of carbon monoxide by organylphosphane—which exclusively affords the *trans*-isomer *(5)* and strengthens the already electronically unfavorable state—leads to metal phosphanes which lose metal halide even more readily.





(5), M = Cr
νCO: 1944(w), 1871(vs)
(Benzene)



(6a), M = Cr, X = S
(6b), M = W, X = S
(6c), M = W, X = Se

On the other hand, attachment of sulfur or selenium [*(6)*] *via* the lone pair on phosphorus, stabilizes the metal-phosphorus bond. Compounds *(6)* are formed without catalytic assistance or thermal induction and cannot be reconverted into *(3)* by strongly basic organylphosphanes (which merely substitute *trans* CO).

The number, position, and intensity of the carbonyl stretching vibrations confirm the square monopyramidal ligand arrangement at the metal atom in *(3)*, *(5)*, and *(6)* (local symmetry C_s). Direct coupling of phosphorus and metal fol-

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Table 1. Physical data of complexes *(3)* and *(6)* [a].

	M.p. [°C] [b] Color	NMR [c] δ^1H (d) [d] $J(^1HC^{31}P)$	δ^{31}P [e] $J(^{31}P^{183}W)$	IR [f] νCO [cm^{-1}]
(3a)	above 85 (dec.)	3.56	421	2020 1973 1952
	golden yellow	1.9		
(3b)	above 84 (dec.)	4.60	394	2022 1971 1952
	ocker yellow	1.6		
(3c)	above 86 (dec.)	4.70	362	2021 1967 1947
	orange-yellow	1.2		
(6a)	above 202 (dec.)	2.72	196	2040 1985 [g]
	green-yellow	0.9		
(6b)	143—145 (dec.)	3.04	89	2052 1975 [g]
	bright yellow	0.8	284	
(6c)	81—83 (dec.)	4.32	62	2048 1972 [g]
	orange-red	0.7	262	

[a] Analytical data consistent with the given formula.
[b] Closed capillary, Cu-block.
[c] Chemical shift [ppm] without exception downfield relative to TMS (int.) or H_3PO_4 (ext.); coupling constants in Hz.
[d] In C_6D_6.—*(6a)* in CS_2, *(6b)* in THF.
[e] In THF.—*(6a)* in C_6H_6, *(6b)* in CD_3CN.
[f] 0.1 mm NaCl liquid cuvettes (uncomp.); *(3)* in cyclohexane, *(6)* in CS_2.
[g] Intense, broad absorptions.

lows as being most likely from $J(^1HC^{31}P)$[7] and is undoubtedly proved, in the case of *(5)* and *(6)*, by $J(^{31}P^{183}W)$. The ^{31}P resonances have unknown negative values and show that the "transition-metal metalation" of PCl_3 leads to a downfield shift of the NMR signals of up to 200 ppm. The magnitude of this effect depends on the nature of the transition metal.

Experimental:

Synthesis of *(3a)*: A suspension of *(1)*, M=Cr[8], (493 mg, 2.20 mmol) in methylcyclohexane (50 ml) is treated with PCl_3 (343 mg, 2.50 mmol) and the mixture stirred vigorously for 7 h at −5 °C. After removal of solvent *in vacuo* the solid residue is extracted with lukewarm pentane and the complex *(3a)* isolated by freezing (−78 °C). Yield: 455 mg (68.2 %).

Synthesis of *(6b)*: A mixture of *(3c)* (1433 mg, 3.29 mmol) and sulfur (105 mg, 3.27 mmol) in CS_2 is stirred for 6 h at room temperature. After removal of solvent *in vacuo*, the orange-yellow residue is extracted with CS_2/*n*-hexane (1 : 1). Freezing at −78 °C affords 275 mg (62.3 %) of powdered *(6b)*.

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CAS Registry numbers:
(1), M=Cr, 12203-12-2; *(1)*, M=Mo, 12107-35-6; *(1)*, M=W, 12107-36-7; *(2)*, M=Cr, 41367-39-9; *(2)*, M=Mo, 12282-32-5; *(2)*, M=W, 12282-35-8; *(3a)*, 60803-47-6; *(3b)*, 60803-48-7; *(3c)*, 60803-49-8; *(4)*, M=Cr, 60803-50-1; *(4)*, M=Mo, 12128-23-3; *(4)*, M=W, 12128-24-4; *(5)*, 60803-51-2; *(6a)*, 60828-72-0; *(6b)*, 60803-52-3; *(6c)*, 60803-53-4; S_8, 10544-50-0; Se, 7782-49-2; PCl_3, 7719-12-2; ^{31}P, 7723-14-0

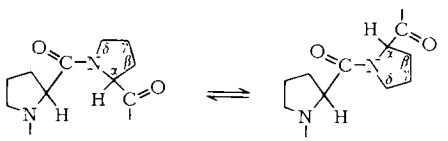
[1] Transition-Metal Substituted VB Element Systems, Part 16.—This work was supported by the Fonds der Chemischen Industrie.—Part 15: *W. Malisch* and *P. Panster*, Chem. Ber., in press.
[2] *R. G. Hayter*, Prep. Inorg. React. *2*, 211 (1965).
[3] *A. Vizi-Orosz*, J. Organomet. Chem. *111*, 61 (1976); *W. Malisch* and *M. Kuhn*, *ibid.* *73*, C 1 (1974) and literature cited therein.
[4] Br_2P-, $C_6H_5(Cl)P$-, and $CH_3(Cl)P$-transition metal systems display an even stronger tendency to eliminate metal halide. Like doubly substituted transition metal-chlorophosphanes they have been detected only in solution.
[5] *L. Maier*, Fortschr. Chem. Forsch. *8*, 1 (1967).
[6] *W. Malisch*, unpublished results.
[7] This coupling cannot be determined in the case of *(3c)* because of its small magnitude.
[8] For *(1)* see *E. O. Fischer*, *W. Hafner*, and *H. O. Stahl*, Z. Anorg. Allg. Chem. *282*, 47 (1955); for *(2)* see *W. Malisch* and *M. Kuhn*, Chem. Ber. *107*, 979 (1974).

NMR Spectroscopic Detection of *cis* and *trans* Peptide Bonds in Unprotected Oligo-L-prolines[**]

By *Manfred Rothe* and *Hans Rott*[*]

Dedicated to Professor Leopold Horner on the occasion of his 65th birthday

Poly-L-proline forms two helix structures which are characterized by the *trans*- and *cis*-configurations of their peptide bonds (polyproline II and I). In the *cis-trans* isomerization the C_α protons of the pyrrolidine ring change their positions relative to the peptide carbonyl group. The isomers can therefore be distinguished on the basis of the chemical shifts of their C_α—H resonances: $\tau_I = 5.48$ ppm, $\tau_{II} = 5.19$ ppm in CD_3COOD.



I: *cis* II: *trans*

In order to examine whether helix formation already occurs in short proline chains and to find out what influence the chain length has on the stabilization of the helical structures, we synthesized molecularly homogeneous, unsubstituted oligomers of the L-proline[1]

H—(Pro)$_n$—OH with $n = 2$ to 40

We found that the tendency to form all-*trans*- and all-*cis*-peptides depends on the chain length of the oligomer and on the solvent. Strong interactions between the solvent (water, carboxylic acids) and the peptide carbonyl groups, *e.g.* by hydrogen bonding[2], stabilize the *trans*-helix, whereas weak interactions (unsubstituted aliphatic alcohols) promote the

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[**] Conformations of Linear Proline Oligomers, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and BASF AG, Ludwigshafen, Germany. Part 3: *M. Rothe*, *R. Theysohn*, *K.-D. Steffen*, *H.-J. Schneider*, *M. Zamani*, *M. Kostrzewa*, and *W. Schindler*, Angew. Chem. *82*, 557 (1970); Angew. Chem. Int. Ed. Engl. *9*, 535 (1970).

cis-helix. The differing strength of the bonding between solvent and peptide carbonyl groups could be determined from small differences in the τ values of the C_α—H resonances (CF_3COOD: 5.10 ppm; CD_3COOD: 5.19 ppm; D_2O: 5.24 ppm; CF_3CD_2OD: 5.26 ppm; CD_3OD: 5.31 ppm). In CD_3COOD and CF_3COOD all oligopeptides have the *trans*-configuration. We found that there is a distinct dependence of the configuration on chain length in the other solvents, di- and triprolines behaving differently from the higher oligoprolines: in D_2O, di- and triproline are in *cis-trans* equilibrium; from $n=4$ onwards only *trans* peptide bonds are formed. In CD_3OD, diproline is completely and triproline extensively *cis* configurated, respectively. The proportion of *cis* bonds ($\tau=5.50$ ppm) passes through a minimum at $n=4$ and increases rapidly with increasing chain length; the all-*cis* configuration is reached at $n>10$. The reverse behavior was observed in CF_3CD_2OD: here diproline is likewise completely *cis* configurated; in the oligomers with $n=3$ to 10, both *cis* and *trans* peptide bonds occur. From $n=12$ onwards we found exclusively *trans* peptide bonds. In the case of C- and N-protected oligoprolines, however, apart from in the first disordered four members, only all-*trans* peptide bonds are found[4]. The ability of di- and triprolines to form *cis* peptide bonds is consistent with the pronounced tendency to form cyclotriprolyls and, particularly, cyclodiprolyls[3].

While only the signal of the *cis*- or *trans*-isomer appears in the range of C_α protons in the ^{1}H-NMR spectra of the polyproline and the oligomers with $n>15$, the spectra of the lower oligomers contain additional resonances which arise from the N- and C-terminal proline residues. The τ values of the C-terminal proline residue depend on the position of the dissociation equilibrium of the carboxyl group, and hence on the solvent (CF_3COOD: 5.1 ppm; CD_3COOD: 5.4 ppm; D_2O, CF_3CD_2OD, CD_3OD: 5.7 ppm).

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German version: Angew. Chem. *88*, 844 (1976)

CAS Registry numbers:
Proline polymer, 25191-13-3; proline repeating unit, 25213-33-6

[1] *M. Rothe* and *R. Theysohn*, Tetrahedron Lett. *1970*, 4063; *M. Rothe* and *J. Mazánek*, *ibid. 1972*, 3795.
[2] *V. Ganser*, *J. Engel*, *D. Winklmair*, and *G. Krause*, Biopolymers *9*, 329 (1970).
[3] *M. Rothe*, *W. Schindler*, *R. Pudill*, *M. Kostrzewa*, *R. Theysohn*, and *R. Steinberger*: Proceedings of the 11th European Peptide Symposium. North Holland, Amsterdam 1971, p. 388.

Crystal Structure of $Te_5O_4F_{22}$[**]

By *Hans Pritzkow* and *Konrad Seppelt*[*]

Sulfur and selenium form the monomeric compounds SOF_4 and $SeOF_4$[1a], whereas in the case of tellurium only polymeric $(TeOF_4)_n$ and oligomers of the type $F_5Te—(OTeF_4)_n—OTeF_5$ have been described[1b]. Little is known about the structures of these compounds. Previously it had been assumed that they contained O—TeF_4—O octahedra coupled *via* oxygen and it is unclear whether the two oxygen atoms occupy the *cis* or *trans* position. Polymeric $(TeOF_4)_n$ is formed in the pyrolysis of $B(OTeF_5)_3$[1b] and in the fluorination of $As(OTeF_5)_3$[2].

$$As(OTeF_5)_3 \xrightarrow{F_2} [AsF_2(OTeF_5)_3] \rightarrow AsF_5 + (TeOF_4)_n$$

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

From the polymeric mixture obtained by the latter reaction we were able to isolate a component having the composition $Te_5O_4F_{22}$. It is a crystalline, sublimable solid which melts at 76 °C; it was characterized by its vibrational, mass, and NMR spectra[2]. A crystal structure analysis has now been carried out on this apparently complicated oxide fluoride of tellurium.

$Te_5O_4F_{22}$ crystallizes tetragonally, space group $I4_1/a$ with the cell parameters $a=8.816(2)$, $c=20.341(6)$ Å and $Z=4$ formula units in the unit cell. The structure was solved with Patterson and difference Fourier syntheses and refined by the method of least squares (1178 independent reflections with $I>\sigma$, all atoms anisotropic) to $R=0.049$.

The compound is made up of isolated $TeF_2(OTeF_5)_4$ octahedra (Fig. 1). Four outer octahedra are coupled *via* their

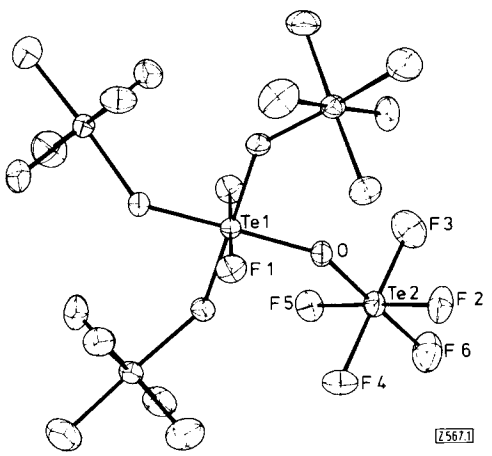

Fig. 1. Molecular structure of $Te_5O_4F_{22}$.

corners to a central octahedron. Limiting tellurium to an octahedral environment and allowing no oxygen double bonds, there are still twelve possible isomers for a molecule of formula $Te_5O_4F_{22}$. Surprisingly, the substance under investigation occurs only in the highly symmetric arrangement. This finding is in accord with the ^{19}F-NMR spectrum of $Te_5O_4F_{22}$.

Since no short intermolecular distances occur, the geometry of the molecule is determined only by intramolecular forces. Remarkably, the tellurium-fluorine bonds in the central octahedron are somewhat longer (1.849 Å) than the others (1.798 to 1.819 Å). The large Te—O—Te angle (139.4°) could be due to repulsion between the tellurium atoms[3]. In the related compounds $Xe(OSeF_5)_2$ and $U(OTeF_5)_6$ the corresponding angles are 125° and 170°, respectively[4]. From these large differences it may be assumed that double bonding leads to stretching of the angle. It would then follow that the d-orbital participation in the case of tellurium is greater than in the case of selenium, while in the case of uranium even f-orbitals participate in the bonding.

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CAS Registry numbers:
$Te_5O_4F_{22}$, 60788-79-6; $TeF_2(OTeF_5)_4$, 60788-81-0

[1] a) *H. Jonas*, Z. Anorg. Allg. Chem. *265*, 273 (1951); *K. Seppelt*, Angew. Chem. *86*, 103 (1974); Angew. Chem. Int. Ed. Engl. *13*, 91 (1974); Z. Anorg. Allg. Chem. 406, *287 (1974)*; *b) F. Sladky*, *H. Kropshofer*, and *O. Leitzke*, J. Chem. Soc. Chem. Commun. *1973*, 134.
[2] *K. Seppelt*, Chem. Ber., in press.
[3] *C. Glidewell*, Inorg. Chim. Acta *12*, 219 (1975).
[4] *L. K. Templeton*, *D. H. Templeton*, *N. Bartlett*, and *K. Seppelt*, Inorg. Chem., in press.

Table 1. Properties of compounds *(3)* and *(4)*. [a] ^{1}H-NMR in C_6H_6. ^{31}P-NMR in CH_2Cl_2.

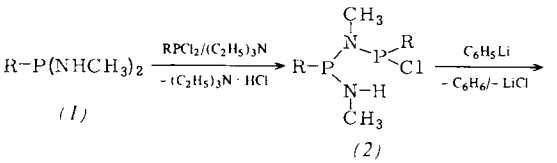
	M.p. [°C]	δ^{31}P [ppm] [a, c] P^{III}	P^{V}	δ^1H [ppm] [a, b] $^2J_{PP}$ [Hz]	NCH_3	$C(CH_3)_3$	J_{PH} [Hz] PNCH	PCCH
(3a)	−4 to −2	−201.7		28.0 [d]	−2.55 (t)	−0.94 [e]	12.3	12.8 [f]
(3b)	110 to 111	−281.7		24.3 [d]	−2.25 (t)	−1.15 [e]	9.0	11.2 [f]
(4a)	144 to 145		−120.1	22.2 [d]	−2.51 (t)	−1.08 [e]	14.5	19.6 [f]
(4b)	subl. above 205		−105.9	9.5 [d]	−2.39 (t)	−1.19 [e]	12.3	19.3 [f]

[a] Shift relative to 85 % H_3PO_4 external or TMS internal standard: δ^{31}P and δ^1H have negative signs for downfield shifts. [b] In C_6H_6. [c] In CH_2Cl_2. [d] Calculated and read off from the $[AX_n]_2$-spin system of the ^{1}H-NMR spectrum. In the case of *(3a)* and *(3b)* only $^2J_{PP}$ could be calculated, so a large error range resulted. [e] $[AX_n]_2$-spin system. [f] $N = |J_{PCCH} + J_{PNPCCH}|$.

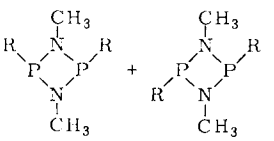
Synthesis and Isolation of *cis*- and *trans*-1,3,2λ^3,4λ^3-Diazadiphosphetidine

By *Otto J. Scherer* and *Günter Schnabl*[*]

In contrast to the *cis*- and *trans*-1,3,2λ^5,4λ^5-diazadiphosphetidine-2,4-dithiones already characterized by crystal structure analysis[1] and the 1,3,2λ^3,4λ^5-diazadiphosphetidin-4-ones or 4-thiones, some of which are detectable in solution as mixtures of *cis*- and *trans*-isomers[2], all the 1,3,2λ^3,4λ^3-diphosphetidines that have been synthesized thus far and investigated NMR spectroscopically exist in only one isomeric form[3]. With the isolation of *(2)*[4] we have now been able to demonstrate for the first time the existence of the postulated intermediates[3b, 5] in some 1,3,2λ^3,4λ^3-diphosphetidine syntheses and have found a method for preparation of *cis*- and *trans*-1,3,2λ^3,4λ^3-diazadiphosphetidines [*(3a)* and *(3b)*].



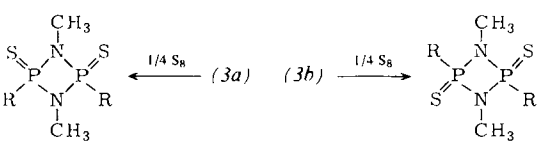
(1) *(2)*



(3a), *cis* *(3b)*, *trans*

R = C(CH$_3$)$_3$

(3b), whose structure was confirmed by a crystal structure analysis[8], shows an unusual downfield shift in the ^{31}P-NMR spectrum (Table 1). Compounds *(3a)* and *(3b)* are oxidized stereospecifically by elemental sulfur (in ice-cold pentane) to the 1,3,2λ^5,4λ^5-diazadiphosphetidin-2,4-dithiones *(4a)* and *(4b)*, respectively, which also differ markedly in their melting points.



(4a), *cis* *(4b)*, *trans*

R = C(CH$_3$)$_3$.

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No transformation into the other isomer could be detected by NMR spectroscopy on warming *(3a)* or *(3b)* to *ca.* 140 °C for several hours.

Experimental:

Synthesis of *(3a)* and *(3b)*: A solution of phenyllithium (52.8 mmol) in ether (44 ml) is added dropwise with stirring to an ice-cold solution of *(2)*[6] (13.0 g, 48.0 mmol) in pentane (250 ml). The mixture is then allowed to warm to room temperature, stirred for a further 3 hours, and filtered on a G3 frit. The filtrate is concentrated in a vacuum and fractionally distilled. *(3b)* sublimes on the cold finger, while *(3a)* drips into the receiver. *(3b)* is purified by resublimation (oil-pump vacuum) and *(3a)* by redistillation in a 10-cm Vigreux column. B.p. 32—34 °C/0.1 torr *(3a)*, subl. temp. 55—70 °C (bath temperature)/0.1 torr *(3b)*.

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CAS Registry numbers:
(2), 60746-25-0; *(3a)*, 60746-26-1; *(3b)*, 60746-27-2; *(4a)*, 60746-28-3; *(4b)*, 60746-29-4; ^{31}P, 7723-14-0

[1] *R. A. Shaw et al.*, Phosphorus *1*, 153 (1971).
[2] Examples: a) *O. J. Scherer* and *G. Schnabl*, Chem. Ber. *109*, 2996 (1976); b) *G. Bulloch* and *R. Keat*, J. Chem. Soc. Dalton Trans. *1976*, 1113.
[3] a) *O. J. Scherer* and *P. Klusmann*, Angew. Chem. *81*, 743 (1969); Angew. Chem. Int. Ed. Engl. *8*, 752 (1969); b) *G. Bulloch* and *R. Keat*, J. Chem. Soc. Dalton Trans. *1974*, 2010; c) *K. W. Muir*, J. Chem. Soc. Dalton Trans. *1975*, 259; also Ref. [2].
[4] *(2)*, which like all other compounds was characterized by elemental analysis, ^{1}H-NMR and mass spectra, and molecular weight determination [*(2)*, *(3a)*, *(3b)*, and *(4a)* cryoscopically in benzene, *(4b)* osmometrically in methylene chloride] forms colorless crystals (m.p. 68 to 70 °C) which reveal the presence of a mixture of rotamers (rotamer A, *ca.* 80 %, $^2J_{PP}$ = 265 Hz; B, *ca.* 20 %, $^2J_{PP}$ = 190 Hz) in the ^{1}H- and ^{31}P-NMR spectra (in C_6H_6).
[5] *R. Keat et al.*, J. Chem. Soc. Dalton Trans. *1973*, 1414.
[6] Prepared from *(1)* [7] and *tert*-$C_4H_9PCl_2$ in pentane at room temperature with triethylamine as HCl acceptor.
[7] *O. J. Scherer* and *P. Klusmann*, Z. Anorg. Allg. Chem. *370*, 171 (1969).
[8] Dr. *S. Pohl*, Bielefeld, private communication.

Synthesis of Cycloheptasulfur Oxide, S_7O[1]

By *Ralf Steudel* and *Torsten Sandow*[*]

Compounds containing cumulated sulfur-sulfur bonds, such as S_8, R_2S_3, or R_2S_4, can be oxidized with trifluoroperoxyacetic acid to sulfoxides (S_8O; R_2S_nO, $n = 3$ or 4)[2]. We have now

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found that cycloheptasulfur[3] reacts smoothly with CF_3CO_3H at -20 °C in dichloromethane to give S_7O in 45% yield:

$$S_7 + CF_3CO_3H \rightarrow S_7O + CF_3CO_2H$$

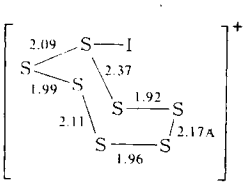
S_7O crystallizes from CH_2Cl_2 as orange, at -80 °C yellow, transparent monoclinic crystals having a density of 2.1$_5$ g·cm^{-3} (25 °C). Elemental analysis and osmometric determination (at 0 °C in CH_2Cl_2) of the relative molecular mass (calc. 240; obs. 244) confirm the formula.

S_7O decomposes completely within 24 h at 25 °C in diffuse daylight, but only within several days in the dark. At -50 °C the compound can be stored for longer periods without decomposition. It melts at 55 °C (SO_2 evolution), and on decomposition at normal pressure gives SO_2 and polymeric sulfur, which according to its Raman spectrum contains only a small amount of S_8. The mass spectrometrically[4] investigated decomposition in a high vacuum proceeds, as in the case of S_8O[5], according to the following equation:

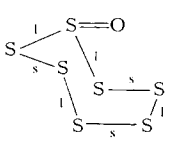
$$S_7O \rightarrow S_2O + \frac{5}{n} S_n$$

The ions SO^+, S_2O^+, and S_n^+ ($n = 1$ to 8; S_2^+ most abundant, followed by S_5^+) were detected, but no molecular ion was observed (sample temperature 60 °C).

The Raman spectrum[4] of S_7O recorded at -90 °C could be assigned by comparison with the spectra of S_7[6] and S_8O[7] and enabled some conclusions to be drawn about the molecular structure. The molecule S_7 belongs to the point group C_1[8], to which S_7O must therefore also belong, *i.e.* all 18 normal vibrations are Raman active. Of these, 17 could be identified (Table 1), *viz.* ν_{SO} (which in the crystal is split into three components)[9], 1 δ_{SSO}, 7 ν_{SS}, and the 8 deformation and torsion vibrations of the ring. Since the spectra of S_7 and S_7O are very similar in the region of the ring deformation vibrations, both compounds must contain rings having the same conformation. On the other hand, there is no similarity in the SS stretching vibrations, a fact which can be attributed to the influence of the oxygen atom (cf. the pair S_8/S_8O[7b, 10]). The SS nuclear separations determined from the wave numbers of the SS stretching vibrations[11] are: 1.93, 1.97, 1.99, 2.11, 2.14, 2.17, and 2.19 Å [three short (s) and four long (l) bonds compared with the single bond length of 2.06 Å[12]]. S_7O



S_7I^+ [13]



S_7O

thus resembles the isoelectronic cation S_7I^+, which was recently isolated as the hexafluoroantimonate and characterized by X-ray structure analysis[13]. The SO nuclear separation obtained from ν_{SO} using valence force constants[15] calculated according to the two-body model[14] is 1.48 Å.

The synthesis of S_7O raises the question whether the hypothetical S_7S, isoelectronic with S_7O and isomeric with cyclooctasulfur, might be considered as a component of liquid or gaseous sulfur.

Table 1. Wave numbers and intensities of the normal vibrations in the Raman spectrum of crystalline S_7O (cm^{-1}; sample temperature -90 °C, spectral split width 1.5 cm^{-1}, intensities: vs very strong, s strong, m moderate, w weak, vw very weak; ν stretching vibration, δ deformation vibration, τ torsion vibration.

1113 vw	ν_{SO}	390 w	δ_{SSO}	209 w	δ_{ring} and τ_{ring}
1102 w		372 w-m	ν_{SS}	193 m	
1098 vw		345 m		165 s	
575 m	ν_{SS}	325 vs		158 m	
534 w		292 s	δ_{ring}	129 w-m	
517 m		281 m			
402 w		232 s			

Experimental

$(CF_3CO)_2O$ (4.4 ml) is added with vigorous stirring at 0 °C to a suspension of H_2O_2 (0.91 g; 80%) in CH_2Cl_2 (95 ml, purified by column chromatography on basic Al_2O_3). The reaction mixture is warmed to 25 °C and stirred until no droplets of H_2O_2 are discernible. S_7 (272 mg) is dissolved in ultrapure CH_2Cl_2 (80 ml) at 0 °C and the solution protected against exposure to light. The CF_3CO_3H solution (5.6 ml) is then added dropwise with stirring within 15 min at -20 °C. The golden-yellow mixture is stirred for one hour and then cooled to -70 °C, whereupon S_7O (130 mg, 45%) crystallizes out. The crystals are collected on a cooled glass frit at -30 °C in the absence of moisture, washed with a little cold CH_2Cl_2, and dried in an oil-pump vacuum. If necessary the product is recrystallized from CH_2Cl_2 (50 ml) by dissolution at 0 °C and cooling to -80 °C.

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CAS Registry numbers:
S_7O, 60828-66-2; $(CF_3CO)_2O$, 407-25-0; S_7, 21459-04-1

[1] Part 45 of Sulfur Compounds. Part 44: *R. Steudel, F. Rose,* and *J. Pickardt*, Z. Anorg. Allg. Chem., in press.
[2] *R. Steudel* and *J. Latte*, Angew. Chem. *86*, 648 (1974); Angew. Chem. Int. Ed. Engl. *13*, 603 (1974); Chem. Ber., in press.
[3] *M. Schmidt, B. Block, H. D. Block, H. Köpf,* and *E. Wilhelm*, Angew. Chem. *80*, 660 (1968); Angew. Chem. Int. Ed. Engl. *7*, 632 (1968).
[4] Perkin-Elmer IR spectrometer 325; Varian Cary 82 Raman spectrometer with krypton laser (647.1 nm); Varian 711 mass spectrometer (70 eV electron energy, 220 °C ion source temperature).
[5] *R. Steudel* and *M. Rebsch*, Z. Anorg. Allg. Chem. *413*, 252 (1975).
[6] *M. Gardner* and *A. Rogstad*, J. Chem. Soc. Dalton Trans. *1973*, 599; *R. Steudel* and *F. Schuster*, unpublished results.
[7] a) *R. Steudel* and *M. Rebsch*, J. Mol. Spectrosc. *51*, 334 (1974); b) *R. Steudel* and *D. F. Eggers*, Spectrochim. Acta *31 A*, 871 (1975).
[8] *I. Kawada* and *E. Hellner*, Angew. Chem. *82*, 390 (1970); Angew. Chem. Int. Ed. Engl. *9*, 379 (1970); *R. Steudel*, Spectrochim. Acta *31 A*, 1065 (1975).
[9] S_7O is readily soluble in CS_2; this solution shows only one SO stretching vibration in the IR spectrum at 1129 cm^{-1}.
[10] *P. Luger, H. Bradaczek, R. Steudel,* and *M. Rebsch*, Chem. Ber. *109*, 180 (1976).
[11] *R. Steudel*, Z. Naturforsch. *30b*, 281 (1975).
[12] *R. Steudel*, Angew. Chem. *87*, 683 (1975); Angew. Chem. Int. Ed. Engl. *14*, 655 (1975).
[13] *J. Passmore, P. Taylor, T. Whidden,* and *P. White*, J. Chem. Soc. Chem. Commun. *1976*, 689 and private communication.
[14] As regards the justification of this approximation, see *R. Steudel*, Z. Naturforsch. *25b*, 156 (1970); *26b*, 750 (1971).
[15] *J. Gillespie* and *E. A. Robinson*, Can. J. Chem. *41*, 2074 (1963).

Formation of Carbenium Ions in the Reaction of Aluminum Chloride with *tert*-Butyl Chloride in Liquid Hydrogen Chloride

By *Franz Kalchschmid* and *Erwin Mayer*[*]

The catalytic action of aluminum chloride in Friedel-Crafts reactions is usually explained in terms of intermediary occurrence of carbenium ions. However, a spectroscopic identifica-

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tion of these intermediates has, to our knowledge, so far proved unsuccessful. At low temperatures weak donor-acceptor complexes between alkyl chloride and aluminum chloride have been detected[1]. In the reaction of *tert*-butyl chloride with $AlCl_3$ at $-78\,^{\circ}C$ a crystalline 1:1 complex could be isolated[2], which according to the ^{1}H-NMR signal of the *tert*-butyl group, however, does not contain a carbocation. Only reaction of alkyl chlorides with SbF_5, FSO_3-SbF_5, and HF-SbF_5 gave stable carbenium ions[1].

We have established that *tert*-butyl chloride reacts with excess $AlCl_3$ in anhydrous liquid hydrogen chloride quantitatively with formation of the carbenium ion *(1)*.

$$C(CH_3)_3Cl + Al_2Cl_6 \rightarrow [C(CH_3)_3^+][Al_2Cl_7^-]$$
(1)

The reaction was carried out in sealed glass ampoules and was complete within a few minutes at 25 °C. *(1)* was identified ^{1}H-NMR spectroscopically at 25 °C (singlet at −4.38 ppm, TMS as external standard; cf. −4.45 ppm for $[C(CH_3)_3^+][Sb_2F_{11}^-]$ in pure SbF_5[3]) and by a low-temperature IR spectrum of the product remaining after removal of the hydrogen chloride at −112 °C[4]. The IR absorptions (2958 cm^{-1} w, 2780 m, 2720 sh, 1452 m, 1285 vs, 1265 vs, 1195 m, 1110 sh, 1068 s, 957 s, 900 s) were very similar to the values published by *Olah*[3, 5] except for differences in intensities and band splitting. From the absence of the intense IR bands of *tert*-butyl chloride it could be concluded that the reaction was quantitative. Investigation of the Raman spectrum was rendered difficult by strong fluorescence of the HCl solution above 400 cm^{-1}; nevertheless, characterization of the anion as $Al_2Cl_7^-$ (bands at 317 cm^{-1} vs, 160 m, 97 m)[6] was possible.

The rate of formation of $[C(CH_3)_3]^+$ depends on the purity and particle size of the $AlCl_3$ employed. For Raman investigations specially purified $AlCl_3$ reacts within hours at −60 °C, less carefully purified samples react only slowly even at −30 °C. The course of the reaction can be followed ^{1}H-NMR spectroscopically by the shift of the *tert*-butyl singlet at −1.94 ppm (*tert*-butyl chloride in HCl at −60 °C) to the value for $[C(CH_3)_3]^+$ (−4.38 ppm). As in investigations carried out by *Olah*, exchange between carbenium ion and unreacted *tert*-butyl chloride leads to only one singlet, whose chemical shift lies between these two values, depending on the concentration.

Solutions of $[C(CH_3)_3]^+[Al_2Cl_7]^-$ in liquid HCl are stable for weeks at 25 °C and discolor only slowly. Solutions stored at −30 °C remain colorless. Solid $[C(CH_3)_3^+][Al_2Cl_7^-]$, obtained by removal of HCl at −112 °C, already decomposes at *ca.* −50 °C.

Reaction of aluminum bromide with *tert*-butyl bromide in liquid HBr likewise furnishes the ion $[(C(CH_3)_3]^+$ (^{1}H-NMR signal at −4.7 ppm). Hence, it should be possible to carry out the first complete investigation of the IR and Raman spectra of the *tert*-butyl cation, since the $[Al_2Br_7]^-$ bands are strongly shifted compared to those of $[Al_2Cl_7]^-$.

Experimental:

The reactions were carried out in sealed glass ampoules. Thick-walled ampoules had to be used since liquid hydrochloride develops a vapor pressure of 60 atm at 36 °C. 5-mm NMR tubes having a wall-thickness of 0.7 mm have proved to be sufficiently stable up to 30 °C. For safety, however, the NMR spectra were recorded at or below −30 °C. Typical concentrations for an NMR experiment: 1 mmol Al_2Cl_6, 0.5 mmol *tert*-butyl chloride, and 7 mmol HCl. The substances were sealed in tubes under vacuum at −196 °C in the absence of moisture. The concentration of *tert*-butyl chloride in this mixture, and hence of the $[C(CH_3)_3]^+$ present after the reaction, was about 1.5 mol/l.

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German version: Angew. Chem. *88*, 849 (1976)

CAS Registry numbers:
(1), 60804-16-2; *tert*-butyl chloride, 507-20-0; $AlCl_3$, 7446-70-0

[1] *G. A. Olah*, Angew. Chem. *85*, 183 (1973); Angew. Chem. Int. Ed. Engl. *12*, 173 (1973); and literature cited therein.
[2] *S. Cesca, A. Priola*, and *G. Ferraris*, Makromol. Chem. *156*, 325 (1972).
[3] *G. A. Olah, E. B. Baker, J. C. Evans, W. S. Tolgyesi, J. S. McIntyre*, and *I. J. Bastien*, J. Am. Chem. Soc. *86*, 1360 (1964).
[4] KBr pellet at −196 °C. Details of this technique for the IR investigation of substances that are unstable at higher temperatures will be published later.
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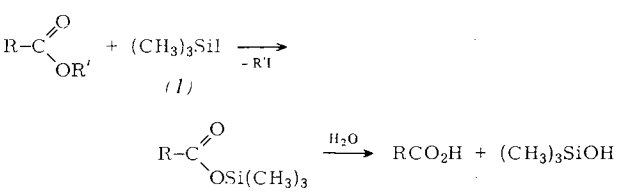
[6] *H. A. Øye, E. Rytter, P. Klaboe*, and *S. J. Cyvin*, Acta Chem. Scand. *25*, 559 (1971).

Cleavage of Esters and Ethers with Iodotrimethylsilane[**]

By *Tse-Lok Ho* and *George A. Olah*[*]

Reagents for nonsaponificative ester hydrolysis are generally powerful nucleophiles which promote O-alkyl cleavage. They are exemplified by lithium iodide/alkylpyridines[1], potassium thiocyanate/dimethylformamide[2], and alkali thiolates in aprotic solvents[3].

We wish to report that iodotrimethylsilane *(1)*[4] is a useful reagent for mild ester cleavage. Selected examples are shown in Table 1. It is seen that difficulties are encountered only with the highly hindered methyl pivalate; in this case a longer reaction time is needed and the yield of free acid is somewhat lower.



(1)

Table 1. Yields of free acid on ester cleavage with iodotrimethylsilane.

R′	R	Reaction time [h]	Yield [%]
CH_3	C_6H_5	2	80
	2-Br—C_6H_4	2	81
	C_6H_5—CH_2	2	78
	C_9H_{19}	2	75
	cyclohexyl	2	80
	$(CH_3)_3C$	18	55
C_2H_5	C_6H_5	4	72
	C_6H_5—CH_2	4	70
C_6H_5—CH_2	C_6H_5	2	86
	cyclohexyl	2	90

The advantages of iodotrimethylsilane over lithium iodide as demethylating agent are: neutral and milder reaction conditions (lower temperature, shorter reaction time) and the absence of solubility problems in aprotic solvents.

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[**] Synthetic Methods and Reactions, Part 29.—This work was supported by the National Science Foundation.—Part 28: *T.-L. Ho, M. Henninger*, and *G. Olah*: Synthesis, in press.

Aromatic aliphatic ethers are also cleaved by *(1)*, although in lower yield. Prolonged heating (24h) of *(2a)*, *(2b)*, and *(2c)*, respectively, with the reagent gives 48% phenol, 22% *o*-cresol, and 40% 1-naphthol. Aliphatic ethers are stable under these conditions. The reactions proceed after the manner of a preferred "hardsoft" interaction, which also explains the known cleavage of ethers with HI.

$$\underset{(2)}{Ar{-}O{-}CH_3} + (1) \xrightarrow[-CH_3I]{+H_2O} ArOH + (CH_3)_3SiOH$$

(a): Ar = C_6H_5
(b): Ar = o-CH_3-C_6H_4
(c): Ar = 1-Naphthyl

Procedure for ester cleavage

A mixture of an appropriate ester (5 mmol) and iodotrimethylsilane (2.0 g, 10 mmol) is heated to 100 °C, with exclusion of atmospheric moisture, for the time period specified in Table 1. The cooled reaction mixture is diluted with ether (25 ml), washed with 0.5 N sodium hydroxide (2 × 30 ml), the alkaline solutions are acidified and extracted with chloroform (2 × 30 ml). The dried extracts give TLC-pure carboxylic acid upon solvent removal.

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German version: Angew. Chem. *88*, 847 (1976)

CAS Registry numbers:
(1), 16029-98-4; *(2a)*, 100-66-3; *(2b)*, 578-58-5; *(2c)*, 2216-69-5; methyl benzoate, 93-58-3; methyl 2-bromobenzoate, 610-94-6; methyl benzeneacetate, 101-41-7; methyl decanoate, 110-42-9; methyl 2,2-dimethylpropanoate, 598-98-1; ethyl benzoate, 93-89-0; ethyl benzeneacetate, 101-97-3; benzyl benzoate, 120-51-4; benzyl cyclohexanecarboxylate, 22733-94-4; benzoic acid, 65-85-0

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Heterocyclic Systems with 12 π-Electrons[**][1]

By *Richard Neidlein* and *Hartmut Seel*[*]

Dedicated to Professor Erich Hückel on the occasion of his 80th birthday

Heterocyclic systems with 12 π-electrons which are iso-π-electronic with phenalenium ions were previously unknown. We report here on the first representatives of this class of compounds, *viz.* the heterocyclic cations of type *(5)*.

Using the preparative route outlined in the scheme below we obtained the orange 2-bromo-5*H*-naphtho[1,8-*bc*]-thiophen-5-one *(4a)* from 3-(chloromethyl)-1-benzothiophene *(1)*[2] *via* the intermediates *(2)* and *(3)*. Reaction of *(4a)* with triethyloxonium tetrafluoroborate in dichloromethane at room temperature afforded the 2-bromo-5-ethoxynaphtho[1,8-*bc*]thiolylium tetrafluoroborate *(5a)* as exceptionally moisture-sensitive, black-red crystals (Table 1).

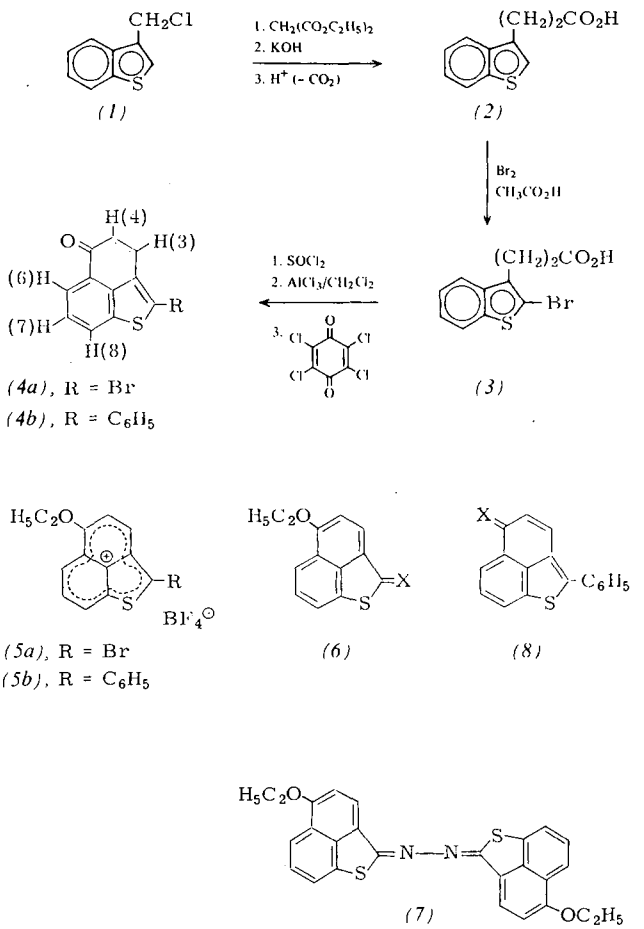

Table 1. Physical properties of compounds *(4)* and *(5)*.

(4a): M.p. 163–164 °C; ^{1}H-NMR ($CDCl_3$): δ = 7.56 ppm (d, H_3, J = 10 Hz), 6.66 (d, H_4, J = 10 Hz), 8.14 (d of d, H_6, J_{ortho} = 8 Hz, J_{meta} = 1 Hz), 7.60 (t, H_7, J = 8 Hz), 7.96 (d of d, H_8, J_{ortho} = 8 Hz, J_{meta} = 1 Hz); IR (KBr): C=O 1625 cm^{-1}, ($CHCl_3$): C=O 1635 cm^{-1}; UV (CH_3OH): λ_{max} = 236 nm (ε = 8640), 265 (12830), 275 (11750), 369 (16620).

(4b): M.p. 137–138 °C; ^{1}H-NMR ($CDCl_3$): δ = 7.65 ppm (d, H_3, J = 10 Hz), 6.55 (d, H_4, J = 10 Hz), 8.13 (d of d, H_6, J_{ortho} = 7 Hz, J_{meta} = 1 Hz), 7.47 (t, H_7), 7.90 (d of d, H_8, J_{ortho} = 8 Hz, J_{meta} = 1 Hz); IR (KBr): C=O 1635 cm^{-1}, ($CHCl_3$): 1630 cm^{-1}; UV (CH_3OH): λ_{max} = 388 nm (ε = 12630).

(5a): ^{1}H-NMR (CD_3CN): δ = 1.68 ppm (t, CH_3—, J = 7 Hz), 4.78 (q, —CH_2—, J = 7 Hz), 7.5–8.8 (H_3, H_4, H_6–H_8); UV (CH_2Cl_2): λ_{max} = 434 nm (ε = 9200).

(5b): M.p. 160–162 °C; ^{1}H-NMR (CF_3COOH): δ = 1.67 ppm (t, CH_3—, J = 7 Hz), 4.84 (q, —CH_2—, J = 7 Hz), 7.6–9.0 (C_6H_5—, H_3, H_4, H_6–H_8); UV (CH_2Cl_2): λ_{max} = 456 nm (ε = 12800).

(5a) reacts with C- or N-nucleophiles in the presence of Hünig base[3] to give compounds of type *(6)*. With hydrazine the violet azine *(7)* is formed.

Reaction of 2-phenyl-5*H*-naphtho[1,8-*bc*]thiophen-5-one *(4b)*[4] with triethyloxonium tetrafluoroborate at 35 to 40 °C leads to the orange-red, very stable salt *(5b)* in 71% yield. This reacts with C- or N-nucleophiles in the presence of Hünig base[3] with elimination of the C_2H_5O group to give products of type *(8)*. The compounds *(8a)* and *(8b)* are iso-π-electronic with phenafulvenes[5] (Table 2).

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[**] Part 1 of Heterocyclic 12 π- and 14 π-Systems. —This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.

Table 2. Physical data of compounds *(6)* to *(8)*.

	X	M.p. [°C]	Yield [%]	Color
(6a)	$(NC)_2C$	249–250	55	red
(6b)	*p*-CH_3—C_6H_4—N	158–159	18	bright yellow
(6c)	C_6H_5—N	119–120	17	bright yellow
(6d)	*p*-$H_5C_2O_2C$—C_6H_4—N	182–183	34	yellow
(6e)	*p*-Cl—C_6H_4—N	184–185	48	yellow
(6f)	*p*-Br—C_6H_4—N	204–205	37	yellow
(6g)	*p*-NC—C_6H_4—N	184–185	35	yellow
(6h)	*p*-O_2N—C_6H_4—N	203–204	52	yellow
(6i)	C_6H_5—CO—NH—N	237–238	54	yellow
(6k)	3-Pyridyl-CO—NH—N	226–227	54	yellow
(6l)	C_6H_5—CH—CO—NH—N	201–202	26	yellow
(6m)	NC—CH_2—CO—NH—N	228–229	53	yellow
(6n)	C_6H_5—NH—N	134–135	49	yellow
(6o)	*p*-O_2N—C_6H_4—NH—N	234–235	36	violet
(6p)	3,5-$(O_2N)_2C_6H_3$—NH—N	280–281	51	violet
(7)		130–132	39	violet
(8a)	$(NC)_2C$	279	16	red-violet
(8b)	2,4,6-Trioxoperhydro-1,3-diazin-5-ylidene	266–267	96	black-red
(8c)	C_6H_5—CO—NH—N	256–257	79	red-yellow
(8d)	2,4-$(O_2N)_2C_6H_3$—NH—N	270–271	92	violet

Experimental:

Synthesis of *(3)*: *(2)* is dissolved in 90% acetic acid (3.5 liters) and the solution warmed to 75°C. A solution of Br_2 (1 mol) in 90% acetic acid is then added dropwise and the mixture stirred for 30 min at 75°C. The cooled solution is poured into 15 liters of water and the resulting precipitate of *(3)* dried and recrystallized from methanol; yield 90%, m.p. 116–117°C.

Synthesis of *(4a)*: A mixture of *(3)* (0.653 mol) and $SOCl_2$ (640 ml) is heated under reflux for 1 h. Excess SO_2Cl_2 is removed, the residue taken up in 4.18 liters anhydrous CH_2Cl_2 and the resulting solution cooled to −10°C and treated portionwise with $AlCl_3$ (0.848 mol). The mixture is stirred for 3 h at −5°C, treated with 60 g $Na_2SO_4 \cdot 10H_2O$ and stirred for a further 4 h at −5°C. It is then washed with H_2O, three times with $NaHCO_3$ solution, and the CH_2Cl_2 solution finally dried over $MgSO_4$. After removal of CH_2Cl_2 the residue (orange-yellow crystals) is recrystallized from acetic acid; yield 84%, m.p. 108–110°C. 0.0754 mol of this substance is heated under reflux for 3 h with 0.468 mol chloranil in 1.5 liters *tert*-butanol. The reaction mixture is then filtered, the *tert*-butanol removed, and the residue taken up in $CHCl_3$; the resulting solution is washed four times with H_2O, four times with 5% NaOH, a further two times with water, and finally dried over $MgSO_4$. After removal of CH_2Cl_2 the remaining orange crystals are recrystallized from acetic acid; yield 75%, m.p. 163–164°C.

Synthesis of *(5a)*: A stirred solution of *(4a)* (1.89 mmol) in anhydrous dichloroethane is treated at 35–40°C with 1.89 mmol triethyloxonium tetrafluoroborate. The resulting deep ruby-red solution is stirred for 20 min, cooled to 0°C, and treated with anhydrous ether, whereupon *(5a)* precipitates as a finely crystalline salt which is used immediately in further reactions. Yield 70 to 80%.

Synthesis of *(5b)*: A stirred solution of *(4b)*[4] (1.91 mmol) in anhydrous dichloroethane (4 ml) is treated at 35 to 40°C with 1.91 mmol triethyloxonium tetrafluoroborate. After 1 h aqueous ethanol is added, whereupon the orange-red salt *(5b)* precipitates. Yield 71%, m.p. 160–162°C.

Synthesis of *(6a)*: $CH_2(CN)_2$ (1.89 mmol) is added to a stirred solution of *(5a)* (1.89 mmol) in anhydrous CH_3CN (10 ml) at room temperature. Hünig base (3.78 mmol) is added to the mixture, which is stirred for 1 h and then allowed to stand overnight at −15°C. Red crystals precipitate; yield 55%.

Synthesis of *(8a)*: A mixture of *(5b)* (1 mmol) and monosodiomalononitrile (1 mmol) in anhydrous tetrahydrofuran (10 ml) is heated under reflux for 24 h. The solvent is removed and the residue chromatographed with benzene an a column packed with silica gel 60 (Merck). After removal of benzene from the eluate *(8a)* is obtained in 16% yield.

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(1), 3216-47-5; *(2)*, 26461-80-3; *(3)*, 10245-72-4; *(4a)*, 60788-83-2; *(4b)*, 10245-71-3; *(5a)*, 60788-85-4; *(5b)*, 60788-87-6; *(6a)*, 60788-88-7; *(6b)*, 60788-89-8; *(6c)*, 60788-90-1; *(6d)*, 60788-91-2; *(6e)*, 60788-92-3; *(6f)*, 60788-93-4; *(6g)*, 60788-94-5; *(6h)*, 60788-95-6; *(6i)*, 60788-96-7; *(6k)*, 60788-97-8; *(6l)*, 60788-98-9; *(6m)*, 60788-99-0; *(6n)*, 60789-00-6; *(6o)*, 60789-01-7; *(6p)*, 60789-02-8; *(7)*, 60789-03-9; *(8a)*, 60789-04-0; *(8b)*, 60789-05-1; *(8c)*, 60789-06-2; *(8d)*, 60789-07-3; 2-bromo-3,4-dihydro-5-oxo-5*H*-naphtho[1,8-*bc*]thiophene, 10245-73-5; triethyloxonium tetrafluoroborate, 368-39-8

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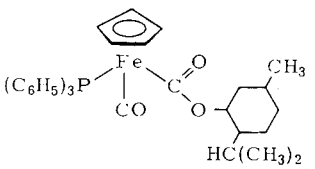
Structure and Absolute Configuration of an Organo-Iron Compound Having Iron as Chiral Center[1]

By *M. George Reisner*, *Ivan Bernal*, *Henri Brunner*, and *Manfred Muschiol*[*]

The absolute configurations are known of optically active organo-Mo compounds with square pyramidal coordination around the metal atom[2] and of ferrocene derivatives[3] in which the metal atom is not the chiral center. We now describe the structure and absolute configuration of compound *(1)*, in which the iron atom is bonded to four different ligands[4].



(1), $[\alpha]_{579} < 0$

Compound *(1)* crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 11.201(3)$, $b = 14.817(7)$, and $c = 18.976(3)$ Å; $V = 3149.36$ Å^3; $d_{exp} = 1.12(2)$ and $d_{calc} = 1.10$ g/cm^3 for a unit cell with four molecules. A total of 4422 independent reflections was collected with a computer-controlled diffractometer using monochromatized Mo-Kα radiation ($\lambda = 0.71069$ Å) to $2\Theta \leq 60°$. The structure was solved and refined using 2194 reflections for which $I(hkl) > 3\sigma[I(hkl)]$. The final $R(F)$ and $R_w(F)$ values were, respectively, 0.066 and 0.072. The absolute configuration of *(1)* was determined by refinement of the entire data set with the two possible enantiomeric configura-

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tions as models and by direct measurement of those 26 Friedel pairs (four measurements for each pair) for which the differences between $F_{calc}(hkl)$, $F_0(hkl)$, and $F_0(\bar{h}\bar{k}\bar{l})$ was largest. Both methods give the same result. The absolute configuration of *(1)*, shown in Figure 1, also confirms the known[5] absolute configurations of the three chiral centers in the menthyl moiety.

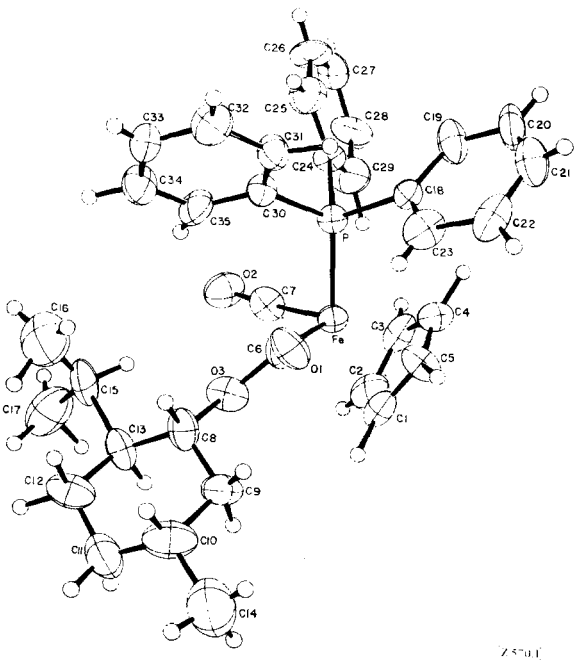

Fig. 1. Structure and absolute configuration of *(1)*. $[\alpha]_{578}<0$.

The Fe—C(C_5H_5) distances average to 2.113(21) Å; other interesting distances are: Fe—P = 2.214(2), Fe—COOR = 1.825(6), Fe—CO = 1.670(7), and C—O (in CO) = 1.206(9) Å. The distances and angles within the triphenylphosphane and menthyl groups compare well with accepted literature values.

With the extension of the *R,S*-system[6] to polyhapto ligands in organometallic complexes[7] the priority sequence of the ligands in *(1)* is $C_5H_5 > P(C_6H_5)_3 > COOC_{10}H_{19} > CO$. The configuration at the Fe atom consequently is (*S*).

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[1] Part 2 of the series "Absolute Configurations of Organometallic Compounds". Part 1: Ref. [2a]. Also Part 45 of the series "Optically Active Transition Metal Complexes". Part 44: *H. Brunner* and *W. Steger*, Bull. Soc. Chim. Belg., in press. *M. G. Reisner* and *I. Bernal* thank the Welch Foundation and the National Science Foundation for support of this study. *H. Brunner* and *M. Muschiol* thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for support of this work.

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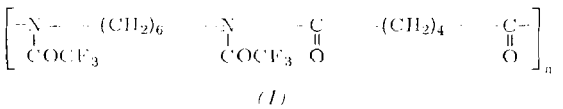
Trifluoroacetylation of Amines with *N*-Trifluoroacetyl-Nylon 66[1]

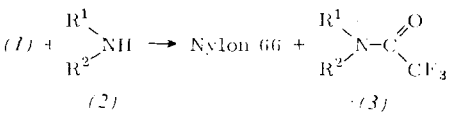
By *Hermann Schuttenberg* and *Rolf C. Schulz*[*]

Reaction of poly(hexamethyleneadipamide) (Nylon 66) with trifluoroacetic anhydride affords high yields of a product which is soluble in tetrahydrofuran (THF), dioxane, chlorinated hydrocarbons, acetone, acetonitrile, or dimethylformamide (DMF). Elemental analysis and IR and NMR spectra are consistent with the substance being a polymer containing the repeating unit *(1)*.



(1)

When treated with water at room temperature the polymer liberates trifluoroacetic acid quantitatively; no detectable degradation of the polyamide chain occurs, either during the synthesis of *(1)* or on treatment with water. The polyamide content of *(1)* can be determined by titration of the liberated trifluoroacetic acid; it agrees up to 98 % with the elemental analysis. Hydrolysis with D_2O[2] furnishes a Nylon 66 extensively deuterated at the nitrogen. Similarly to low molecular *N*-trifluoroacetyl compounds[3], *(1)* can also be employed for the trifluoroacetylation of amines *(2)*.



(2) *(3)*

Table 1. Reactions of *(1)* with amines *(2)* for the preparation of trifluoroacetamides *(3)*. Reaction medium: acetonitrile; room temperature, duration of reaction 12 h; yields and melting points of crude products.

Amine *(2)*	Yield of *(3)* [%]	M.p. [°C] [Lit.-m.p.]	Ref.
Benzylamine	91	73–74 [74–75]	[5]
L-(−)-α-Methylbenzylamine	93	95–96 [96–98]	[6]
Aniline	89	86–87 [89–90]	[5]
n-Hexylamine	95	3–4 [a]	[5]
Hexamethylenediamine	96	119–120 [121–123]	[5]
Piperidine	95	[a]	[5]
p-Nitroaniline	40	[a]	[7]

[a] Identified by comparison of the IR spectra and by gas chromatography with authentic samples.

To carry out the reaction, *(1)* is suspended in acetonitrile. During the course of the reaction Nylon 66 is formed and can be easily separated by filtration. On concentrating the filtrate the corresponding trifluoroacetamide *(3)* is obtained (see Table 1).

Remarkably, *(1)* reacts only slowly, if at all, with some amines, even though these amines react readily with trifluoroacetic anhydride. This selectivity can be exploited for the separation of mixtures of amines. Alcohols can likewise be converted into the trifluoroacetyl derivatives with *(1)*.

Experimental:

Synthesis of *(1)*: Trifluoroacetic acid anhydride (10 ml) is added with vigorous stirring at 0 °C to a suspension of finely

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powdered poly(hexamethyleneadipamide)[4] in chloroform (50 ml). The mixture is allowed to warm slowly with continuous stirring to room temperature; after about 6 h a clear solution is obtained which is then added dropwise to 300 ml ether. Stirring is continued for a further 2 h before the precipitated polymer is separated by decantation, washed with ether, filtered, and dried in a vacuum. Yield 6.5 g (95%). IR (film): $\nu_{CO} = 1715\ cm^{-1}$; no NH band, no amide II band. ^{1}H-NMR ($CDCl_3$): $\delta = 3.73$ (4H), 2.87 (4H), 1.76; 1.45 (m, 12H) ppm.

Analysis: *(1)* (60 to 95 mg) is dissolved in THF (10 ml) and treated with water (0.5 ml). The mixture is stirred for 12 h at room temperature and the liberated trifluoroacetic acid titrated potentiometrically with 0.1 N NaOH (without separation of precipitated Nylon 66).

Reaction with amines: *(1)* (230 mg, 0.55×10^{-3} mol) is added to a solution of the amine (1 mmol) in acetonitrile (5 ml; previously dried over CaH_2). The mixture is stirred at room temperature for 12 h, centrifuged, and the residue washed twice with 5 ml acetonitrile. Concentration of the combined solutions furnishes the trifluoroacetamide *(3)*.

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CAS Registry numbers:
Benzylamine, 100-46-9; L-(−)-α-methylbenzylamine, 2627-86-3; aniline, 62-53-3; *n*-hexylamine, 111-26-2; hexamethylenediamine, 124-09-4; piperidine, 110-89-4; *p*-nitroaniline, 100-01-6; *N*-benzyltrifluoroacetamide, 7387-69-1; *N*-(α-methylbenzyl)trifluoroacetamide, 39995-51-2; *N*-phenyltrifluoroacetamide, 404-24-0; *N*-hexyltrifluoroacetamide, 687-09-2; *N,N'*-hexanediylbis(trifluoroacetamide), 14815-14-6; 1-(trifluoroacetyl)piperidine, 340-07-8; *N*-(*p*-nitrophenyl)trifluoroacetamide, 404-27-3

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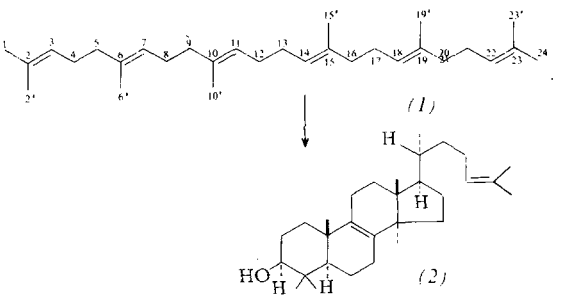
The Crystal Structure of Squalene

By *Josef Ernst, William S. Sheldrick*, and *Jürgen-Hinrich Fuhrhop*[*]

The *in vivo* and *in vitro* cyclization of squalene *(1)* to lanosterol requires epoxidation of a terminal double bond. This reaction proceeds regioselectively only in polar solvents, *e.g.* in glycol dimethyl ether/water mixtures. *Van Tamelen*[1] therefore formulated a coiled structure for *(1)* in that type of media which ought to be stabilized by hydrophobic interactions and in which the inner double bonds would be protected from chemical attack.

In order to check this hypothesis we have subjected squalene crystals which had been obtained from methanol/ether (5:2) to an X-ray structure analysis.

After several recrystallizations at −17 to −30 °C we obtained monoclinic crystals having a melting range −4.8



(1)

(2)

to −5.2 °C which could be easily manipulated in a cold stream of nitrogen and measured in the four-circle diffractometer fitted with low-temperature equipment.

Space group $P2_1/n$ with $a = 7.660(23)$, $b = 6.281(2)$, $c = 28.492(9)$ Å; $\beta = 93.17(9)°$; $Z = 2$; $d_{calc} = 1.00\ g\ cm^{-3}$. The structure was solved by direct methods and refined to $R_w = 0.093$ for 1035 independent reflections (Syntex $P2_1$, $F \geq 4.0\sigma(F)$). The positions of the hydrogen atoms could be located in difference Fourier syntheses and were afterwards included as fixed parameters in the final refinement cycles. The carbon atoms were assigned anisotropic temperature factors.

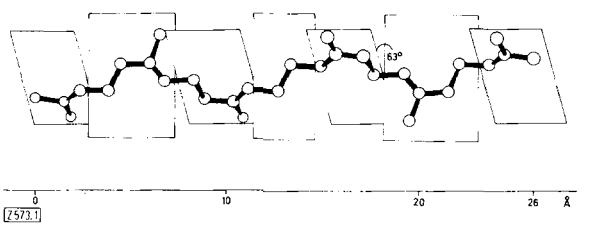


Fig. 1. Projection of the squalene molecule onto the best plane through carbon atoms 3,4,5,6,6',7,8,11,12.

The molecular structure (Fig. 1) shows C_i symmetry and a stretched conformation. The symmetric unit can be represented as sharing two planes which are at an angle of 62.8° to each other. Carbon atoms 3,4,7,8,11, and 12 lie on the lines of intersection. Conformation and orientation of the molecules in the crystal lattice (Fig. 2) are determined by the steric interactions between methyl and methylene groups.

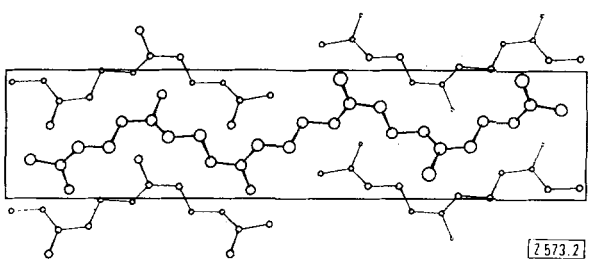


Fig. 2. Projection along the [100] axis.

The structure resembles that of the squalene hexahydrochloride[2] and of the monomeric unit of "crystalline rubber"[3].

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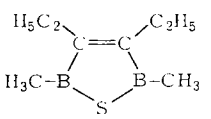
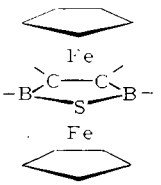
μ-Thiadiborolenebis(η-cyclopentadienyliron)—Preparation and Structure of a New Triple-Decker Sandwich Complex[1]

By *Walter Seibert, Thomas Renk, Klemens Kinberger, Manfred Bochmann*, and *Carl Krüger*[*]

3,4-Diethyl-2,5-dimethyl-1,2,5-thiadiborolene *(1)* serves as a bridging ligand to form the triple-decker complex *(1)*·$[Mn(CO)_3]_2$ with the one-electron donor fragment $Mn(CO)_3$[1]. We now describe the compound *(1)*·$[Fe(C_2H_5)]_2$ *(2)* which is formed on reaction of *(1)* with $[\eta\text{-}C_5H_5Fe(CO)_2]_2$ in mesitylene at 160°C.



(1)



(2)

The triple-decker sandwich structure follows from the analytical and spectroscopic data of *(2)*, which is air-stable, degraded by HI, and first detected in the mass spectrum[2]. The molecular ion ($I_{rel}=88$) is accompanied at 70eV by the fragments $\{M-CH_3\}^+$ (8), $\{M-(C_2H_5C)_2BCH_3\}^+$ (11), $(C_5H_5Fe)_2BCH_3^+$ (11), $C_5H_5FeSB(CH_3)_2^+$ (12), $(C_5H_5)_2Fe^+$ (100), and $C_5H_5Fe^+$ (26).

The crystal structure of *(2)* was deduced from 4072 reflections [1921 unobserved (2σ), cell data: $a=8.729(1)$, $b=16.800(2)$, $c=13.474(2)$ Å, $\beta=72.20(1)°$, $Z=4$, space group $P2_1/c$, $R=0.059$]. The result is shown in Figure 1. The Fe—Fe distance [3.236(1) Å] is considerably shorter than the Mn—Mn distance in the triple-decker complex *(1)*·$[Mn(CO)_3]_2$ [3.506(1) Å][3] and than the Ni—Ni distance in $(C_5H_5)_3Ni_2^+$ [3.576 Å][4]. The central thiadiborolene ring *(1)* is planar. Its geometry corresponds to earlier results[5]. Both cyclopentadienyl rings display rotational disorder.

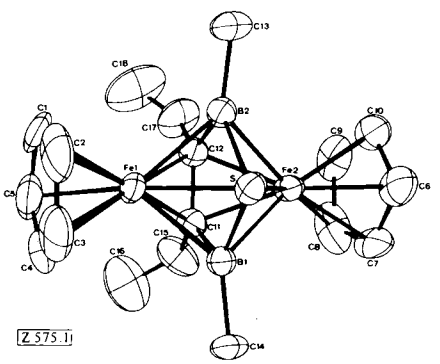


Fig. 1. Crystal structure of the complex *(2)*.

In the ^{1}H-NMR spectrum [$\delta=3.43$ (s, 10), 2.67 (q, 4), 1.62 (s, 6), and 1.48 (t, 6) ppm (in CS_2 *vs.* internal TMS)] the quartet establishes the magnetic equivalence of the methylene protons and hence—as for *(1)*·$[Mn(CO)_3]_2$—the triple-decker structure. The ^{11}B-NMR signal at $\delta=12.0$ ppm [in CS_2 *vs.* external $BF_3\cdot O(C_2H_5)_2$; *(1)*: $\delta=66.0$ ppm] indicates strong electronic shielding of the boron atoms.

Complex *(2)* is formally derived from the red triple-decker sandwich[6] 1,7,2,3-$(\eta\text{-}C_5H_5Co)_2C_2B_3H_5$ by replacement of the 5-B atom by sulfur, requiring a transition from Co-d^6 to Fe-d^6. However, the electronic structure of the green compound *(2)* and that of the green μ-borolebis(η-cyclopentadienyliron)[7] should rather be comparable with that of the green 1,7,2,4-isomer of $(\eta\text{-}C_5H_5Co)_2C_2B_3H_5$. In the Fe and Co triple-decker sandwich compounds three 6 π electron ligands are held together by two d^6 metal ions. These are 30-electron triple-decker complexes, whereas $(C_5H_5)_3Ni_2^+$[8] has 34 valence electrons[9].

Procedure:

Synthesis of *(2)*: $[C_5H_5Fe(CO)_2]_2$ (4.73 mmol) and *(1)* (4.73 mmol) are heated at 160 to 170°C in mesitylene (50 ml) for 8 h. Precipitated iron (0.32 g) is filtered off, the solvent removed, and the residue worked up by chromatography (silica gel/pentane). Sublimation of ferrocene (0.5 g) from the eluate is followed by that of *(2)* at 90°C/0.1 torr: dark green crystals, dec. 230°C (from pentane, at −20°C), yield 11 %.

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CAS Registry numbers:
(1), 54677-51-9; *(2)*, 60860-91-5; $[C_5H_5Fe(CO)_2]_2$, 12154-95-9

[1] Part 2 of Triple-Decker Compounds.—This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 1: *W. Siebert* and *K. Kinberger*, Angew. Chem. *88*, 451 (1976); Angew. Chem. Int. Ed. Engl. *15*, 434 (1976).

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Photoisomerization and Photocleavage of Bicyclo-[4.2.0]octa-2,4-dienes[**]

By *Gerd Kaupp* and *Ernst Jostkleigrewe*[*]

Neither simple nor more sophisticated theoretical approaches can as yet explain the rather unclear and, in part, contradictory results of the photolysis of numerous [2+2]cycloadducts of benzene. We report here on the photolysis of the model compounds *(1a)*[1], *(1c)*[2], *(6a)*[3], and *(6b)*[3].

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Dr. *H. Fritz* (Ciba-Geigy AG, Basel) for recording the ^{13}C-NMR spectra.

In the bicyclo[4.2.0]octa-2,4-dienes *(1)* and *(6)* the valence-tautomerism equilibria with *(2)* and *(7)*, respectively, lie wholly on the side of the bicycles. ^{1}H- and ^{13}C-NMR spectra at -40 to 50°C verify this observation[4]. The photolyses of *(1)* and *(6)* lead without competing fluorescence ($\Phi_{fl} < 10^{-4}$) to cleavage and isomerization reactions with high quantum and product yields (see Table 1). First of all, the allylic or bisallylic four-membered ring bonds are cleaved reversibly. The former corresponds to the stereochemically demonstrated two-step mechanism of cleavage of benzo-annelated derivatives[5]; the latter presumably leads directly to the cyclooctatrienes *(2)* and *(7)*[6], which react further with ring opening to give the octatetraenes *(4)*[7]. Compound *(4a)* is protected from reverse reactions to *(1a)* or *(6a)* by secondary photolyses, which generally terminate at the all-*trans* isomer *(5a)* are formed thermally. As expected, the increased yields thus obtained are wavelength dependent (best results at 253.7 nm).

The data quoted in Table 1 can be interpreted as follows: In the case of the anhydride *(6b)* the bisallylic four-membered ring bond is not cleaved, apparently because the five-membered ring restricts the conformational flexibility necessary for ring expansion to *(7b)* too strongly. When additional rings are absent, as in *(1a)*, *(1c)*, and *(6a)*, cleavage competes with valence isomerization to cyclooctatrienes after absorption of light. The data given in Table 1 show that cleavage competes all the more effectively the more the steric hindrance is relaxed by the initial formation of the diradical [*(3)*]. The reverse reactions afford the most convenient route so far to the syntheses of *(1a)* and *(6a)* from *(4a)*.

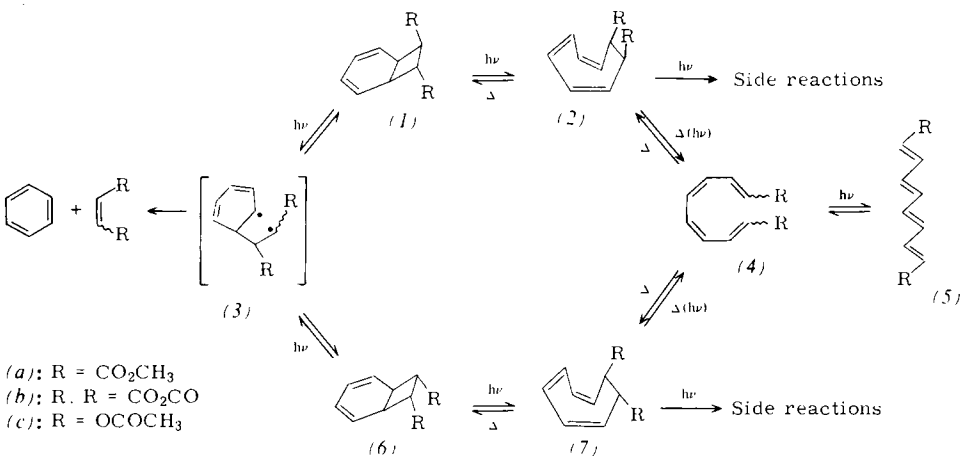

Table 1. Products of the photolysis of bicyclo[4.2.0]octa-2,4-dienes in acetonitrile at 20°C [a].

Compound	λ_{max} (nm) (ε)	Benzene Yield [%]	(4)⇌(5) Yield [%]	Cleavage / Isomerization	Quantum yield [b]
(1a)	273.5 (3500); 295 (sh)	80–85	12–15	5.6	0.50
(6a)	273.5 (3500) 295 (sh)	70–75	22–25	3.0	0.56
(6b)	274.5 (3350)	100	0.0		0.56
(1c)	262 (sh); 267 (3800) 286 (sh); 291 (sh)	10–11	47 [c]	<0.2	0.43 [d]

[a] Saturated with N_2 or air; at 300, 274 or 253.7 nm; complete conversion.
[b] Decrease of *(1)* or *(6)* and increase of benzene and *(5)*; the time-dependent *cis,trans* ratios were taken into consideration with the aid of band positions and ε values.
[c] Maximum enrichment because of the photolability of *(5c)*.
[d] Measurement at -10°C; $\lambda_{max} = 275$ (sh), 286 (sh), 297, 309.5 (ε = 60000), 323 nm.

[CH_3CN: $\lambda_{max}(\varepsilon) = 304$ (sh, 22000), 319 (sh, 44000), 332.5 (67000), 348.5 nm (61500)]. A lowering of temperature is necessary only in the case of *(4c)* (see Table 1).

The formula scheme is confirmed by photolyses at -190°C: the yields of benzene remain unchanged (excitation at 300 and 274 nm), *i.e.* the reactivity of *(3)* is undiminished. The thermal secondary reactions of the intermediates *(2a)*, *(2c)*, and *(7a)*, on the other hand, are frozen in at -190°C. The yields of *(4)* quoted in Table 1 can no longer be achieved by secondary *photolyses* of *(2)* and *(7)* (0.1, 5, and 4% *(4)* from *(1a)*, *(1c)*, and *(6a)*). If the solution is warmed before all of the cyclooctatriene [*(2)*, *(7)*] has been consumed in the secondary photolyses, considerable amounts of *(4)*

Experimental:

cis,cis,cis,trans-(4a) and *trans,cis,cis,trans-(4a)*: The cooled solution of cyclooctatetraenedilithium (prepared from 15 g COT and 2.1 g Li) in 500 ml ether/THF (9:1)[8] is added dropwise over a period of 1 h at -60°C under argon to a solution of methyl chloroformate (47 g) in 300 ml ether. The mixture is stirred for 1 h at -60°C and 12 h at 20°C; it is then filtered, concentrated in a rotary evaporator, and the resulting residue treated with 300 ml cold methanol to initiate crystallization: 1.1 g *cis,cis,cis,trans-(4a)* [m.p. 112°C; ^{1}H-NMR (C_6D_6): two OCH_3 signals, $\delta = 3.39$ and 3.45 ppm]. The filter residue is stirred in 500 ml water. 3.0 g of dry residue is isolated,

extraction of which with 31 boiling petroleum ether (b.p. 30—50°C; duration ca. 1 min) and cooling to −30°C affords 1.3 g *trans,cis,cis,trans-(4a)*[9] in the form of fine needles [m.p. 118°C; ^{1}H-NMR (C_6D_6): one OCH_3 signal, $\delta = 3.44$ ppm, $\Delta\nu_{1/2} \leq 0.6$ Hz; UV(CH_3CN): $\lambda_{max}(\varepsilon) = 300$ (sh, 20500), 314 (36000), 327 (48300), 343 nm (40500)].

Synthesis of *(1a)* and *(6a)*:

Solutions of *trans,cis,cis,trans-(4a)* and *cis,cis,cis,trans-(4a)*, respectively, in benzene are heated to 80°C for 2 h [*(1a)* can also be obtained from the dried crude product by hot-vapor extraction with petroleum ether (b.p. 50—80°C; 10 h)]. Yields after molecular distillation (5×10^{-4} torr, bath 40°C, condensate −20°C): at least 90%.—*(1a)*: m.p. 34°C; ^{1}H-NMR ($CDCl_3$): two OCH_3 signals, $\delta = 3.70$, 3.72 ppm; ^{13}C-NMR: 12 signals.—*(6a)*: m.p. 24°C; ^{1}H-NMR ($CDCl_3$): one OCH_3 signal, $\delta = 3.70$ ppm; ^{13}C-NMR: 6 signals.

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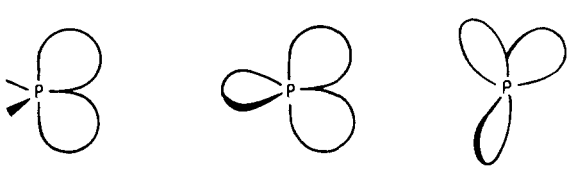
A Tricyclic Phosphorane with Axial Annelation[1]

By *Alfred Schmidpeter*, *Dietmar Schomburg*, *William S. Sheldrick*, and *Josef Helmut Weinmaier*[*]

In phosphoranes having a bicyclo[3.2.0]heptane or bicyclo[3.3.0]octane skeleton the two rings incorporating the trigonal-bipyramidal bridgehead phosphorus always adopt an approximately or precisely meridional spatial arrangement *(A)*[2–4]. The axis of the bipyramid is then bent towards the bond common to the two rings, and the angle between the other two equatorial bonds is consequently[3] reduced to 110—113°. The question arises: Will this narrowing of the angle suffice to accommodate a further small ring in the otherwise avoided diequatorial orientation *(A')* or will an additional small ring once again assume the axial-equatorial position and thus impose the *per se* less favorable facial arrangement *(B')* of the bicyclic system?



(A) *(A')* *(B')*

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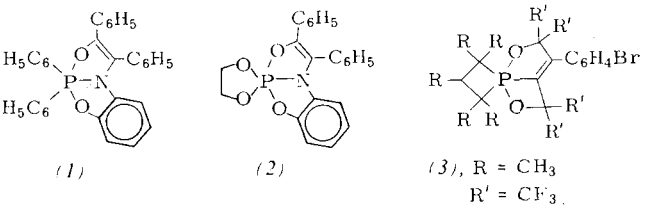
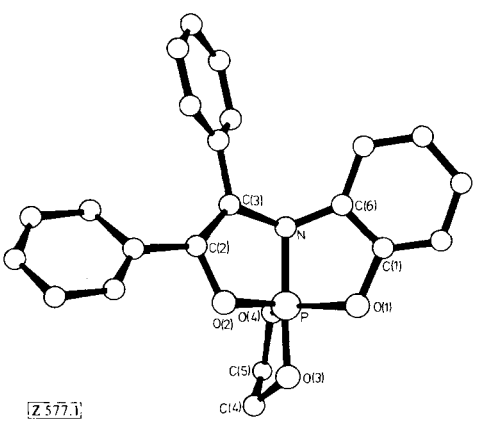
We have found that compounds in which pentacovalent phosphorus serves as bridgehead and spiro center of three five-membered rings can readily be prepared by the method described for the synthesis of *(1)*[5]. One of the resulting products, *viz. (2)*, has been subjected to structural analysis[6].



(1) *(2)* *(3)*, R = CH_3, R' = CF_3

Figure 1 shows that the axial annelation *(B')* occurs in *(2)*, and is particularly obvious from the drastic difference in the N—P—O^3 and N—P—O^4 angles which would actually be equivalent on the basis of the molecular skeleton (Table 1). All the angles at the phosphorus atom can be described to a good approximation in terms of an 85% transition from the meridional arrangement *(A')* of the bicyclic to the facial arrangement *(B')*, as the angles in *(1)* had likewise been described in terms of a 15% transition[2]. Since the two rings in facial orientation are bent towards each other the bridgehead nitrogen is not planar, as is usually the case[2–4], but slightly pyramidal (sum of the angles = 353°).



[Z 577 IE]

Fig. 1. Molecular structure of 8,8-(1,2-ethanediolato)-2,3-diphenyl[1,3,2λ^5]oxazaphospholino[2,3-*b*]benzo[*d*][1,3,2λ^5]oxazaphospholine *(2)*.

Table 1. Bond angles [°] at phosphorus and lengths [Å] of bonds emanating from phosphorus and the adjacent bonds in *(2)*, as compared with the equivalent bonds in *(1)*.

	(2)	*(1)*		*(2)*	*(1)*
O^1—P—O^2	134.0(1)	171.6(3)	P—O^1	1.637(2)	1.763(5)
O^1—P—O^3	86.9(1)		P—O^2	1.635(2)	1.700(5)
O^2—P—O^3	89.6(1)		P—N	1.755(2)	1.703(6)
O^1—P—O^4	115.6(1)		P—O^3	1.654(2)	
O^2—P—O^4	110.4(1)		P—O^4	1.595(2)	
O^1—P—N	89.3(1)	87.6(3)	O^1—C^1	1.395(4)	1.347(8)
O^2—P—N	88.4(1)	86.6(3)	O^2—C^2	1.413(3)	1.376(5)
N—P—O^3	172.4(1)		N—C^6	1.400(3)	1.421(8)
N—P—O^4	93.5(1)		N—C^3	1.406(3)	1.427(5)
O^3—P—O^4	94.1(1)		O^3—C^4	1.421(4)	
			O^4—C^5	1.446(5)	

The difference between the structures *(A')* and *(B')* is also seen in the bond lengths of the bicyclic skeleton of *(1)* and *(2)*. The PO^1 and PO^2 bonds, which are axial in *(1)* and equatorial in *(2)*, are shortened by 8 and 4% respectively, and the PN bond which is equatorial in *(1)* and axial in *(2)* grows longer by 3%. Concomitantly, the adjacent OC bonds become 3% longer, and the NC bonds 2% shorter. The PO bonds of the dioxaphospholane ring differ from each

other by 4%, one being axial and the other equatorial, and the adjacent CO bonds by 2% in the opposite sense.

Structure *(B')* would indicate the four protons of the dioxaphospholane ring *(2)* to differ from each other; in solution, however, they are found to be equivalent by NMR. Hence *(B')* must exist in mobile equilibrium with other structures [including *(A')*] in solution.

In a very recent publication[7], *Trippett et al.* describe the phosphorane *(3)*, which, having the same structural alternatives *(A')/(B')*, adopts the C_s structure *(A')*, presumably owing to the greater difference in electronegativity between the atoms exchanging positions: On going from *(A')* to *(B')* an O,O pair must relinquish its apical position to on O,N pair in the case of *(2)*, but to a C,C pair in the case of *(3)*.

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[1] Four- and Five-Membered Phosphorus Heterocycles, Part 20. This work was supported by the Fonds der Chemischen Industrie.—Part 19: *J. Luber* and *A. Schmidpeter*, Chem. Ztg., in press.

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[6] *(2)*, m.p. 140°C; $\delta^{31}P = 16.4$ ppm *vs.* H_3PO_4 (in CH_2Cl_2); $\delta^1H(C_2H_4) = 4.17$ ppm, d, $J_{POCH} = 14.1$ Hz; monoclinic crystals, $P2_1/n$ with $a = 10.173(2)$, $b = 8.988(2)$, $c = 21.053(4)$ Å, $\beta = 101.69(2)°$, $Z = 4$, $d_{calc} = 1.38$ g cm^{-3}. The structure was solved by direct methods and refined to $R = 0.053$, $R_w = 0.047$ for 2602 independent reflections [$I \geq 2.0(I)$].

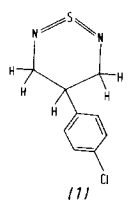
[7] *H. A. E. Aly, J. H. Barlow, D. R. Russel, D. J. H. Smith, M. Swindles*, and *S. Trippett*, J. Chem. Soc. Chem. Commun. *1976*, 449.

X-Ray Structure Analysis of a 4,5-Dihydro-3H-1λ⁴,2,6-thiadiazine

By *Alfred Gieren* and *Franz Pertlik*[*]

X-ray structure analyses of non-cyclic sulfur diimides[1] led to the conclusion that the S^{IV}=N bond lengths (*ca.* 1.53 Å) are independent of the substituents at the SN_2 group and of the configuration at the S=N bonds.

We have now carried out an X-ray structure analysis of the cyclic sulfur diimide 4-(4-chlorophenyl)-4,5-dihydro-3*H*-1λ⁴,2,6-thiadiazine *(1)*[2].



(1)

The compound crystallizes from ethanol in the monoclinic space group $P2_1/n$; lattice constants: $a = 12.58_1$, $b = 10.95_6$, $c = 7.27_7$ Å, $\beta = 103.0_9°$; $D_{exp} = 1.44_1$ g·cm^{-3}, $D_{X\text{-ray}} = 1.45_7$ g·cm^{-3}; $Z = 4$. 1876 independent reflections were measured on an automatic single crystal diffractometer with Cu-K_α radiation up to a maximum θ value of 70° (5-value measurement, θ/2θ scan); 183 reflections were unobserved ($I \leq 2\sigma_I$). The structure was solved by direct methods. All atoms (except H) could be located by an E-Fourier synthesis with the 300 largest E-values. Refinement by the method of least squares (full matrix), first using isotropic and then anisotropic temperature parameters initially gave an *R* value of 8.2%. At this stage of the refinement all hydrogen atoms could be located in a difference Fourier synthesis. On inclusion of the H-atoms with isotropic thermal parameters the refinement converged at an *R* value of 4.1%.

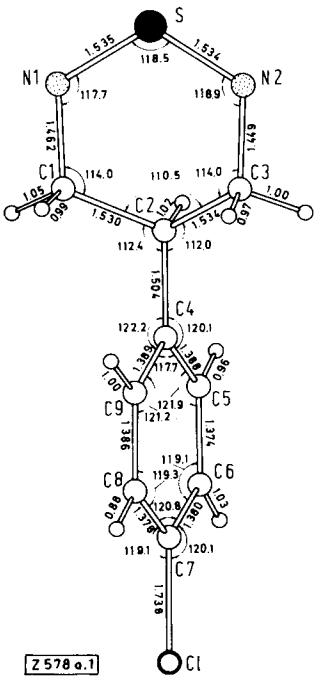


Fig. 1. Molecular structure of 4-(4-chlorophenyl)-4,5-dihydro-3*H*-1λ⁴,2,6-thiadiazine *(1)*. The standard deviations of the given bond lengths vary between 0.003 and 0.005 Å (except C—H: 0.03–0.04 Å), those of the angles between 0.2 and 0.3°.

Figure 1 shows the molecular structure. The ring containing the SN_2 group has a half-boat conformation with the apex at C-2. The *p*-chlorophenyl moiety occupies an equatorial position at C-2 and is orientated almost perpendicularly to the best plane through the heterocyclic ring. The best planes through the coplanar atoms of the two six-membered rings are at an angle of 84° to each other. To a good approximation the molecule contains a plane of symmetry perpendicular to the heterocyclic ring in the plane of the *p*-chlorophenyl ring. The cause of the half-boat conformation is the coplanarity of the sulfur diimide group with the substituents at the nitrogen atoms. In the meantime the same conformation has been found in the $S_3N_3O_4$ anion[3] and in a cyclotetraphosphazene bridged by a sulfur diimido group[4], in which the SN_2 group is likewise part of a six-membered ring.

The length of the S=N double bond is 1.534 Å and agrees within limits of error with the S=N bond lengths in the reference compounds. Since the substituents at the N atoms in *(1)* do not allow π-interaction with the SN_2 system it can be concluded from the above agreement that the length of the S^{IV}=N bond in organic sulfur diimides is independent of the nature of the substituents, even though the reactive behavior of the SN_2 group is subject to a distinct substituent effect. The configuration at the S^{IV}=N double bond also has no influence on the bond length.

The angle at the sulfur atom is 118.5° and obviously varies only within narrow limits. In the open-chain reference compounds it is 117°[1a] and 115°[1b], in the cyclic compounds 119°[3,4].

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The nitrogen atoms of the SN_2 group are sp^2 hybridized, which follows not only from the bond angles at the N atoms (118.3°), but also from the N—C bond lengths (1.455 Å). These bond lengths correspond to the value for N—C single bonds of the type sp^2-sp^3. The angles at C-1 and C-2 are about 4.5° wider than an ideal tetrahedral angle.

The structure of *(1)* contradicts a "double ylide" structure[5] in sulfur diimides.

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CAS Registry numbers:
(1), 60840-53-1

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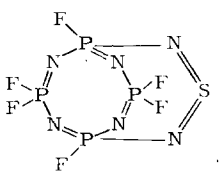
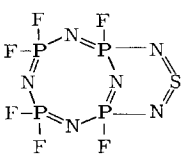
The Structure of a Cyclotetraphosphazene Bridged by a Sulfur Diimido Group

By *Alfred Gieren, Bernhard Dederer, Herbert W. Roesky*, and *Enno Janssen*[*]

The synthesis of a novel cyclotetraphosphazene bridged by a sulfur diimido group has recently been reported[1]. The constitution *(1a)* was proposed for the compound. Such a constitution assumes a non-planar arrangement of the P—N=S=N—P system and would be inconsistent with recent X-ray structure analyses[2, 3], which indicate a coplanar arrangement of the SN_2 system and the substituents at the nitrogen atoms as being characteristic for sulfur diimides. We have therefore carried out an X-ray structure analysis of *(1)*.



(1a)



(1b)

The crystals of *(1)* obtained by sublimation crystallize in the monoclinic space group $P2_1/b$ with $a = 9.43_6$, $b = 20.10_2$, $c = 11.62_2$ Å; $\gamma = 103.5_2°$. The unit cell contains eight formula units (2 formula units/asymmetric unit). The crystal structure has an additional pseudosymmetry of the space group B2/b, since reflections of the type $h+l=2n+1$ are on average much weaker than those of the type $h+l=2n$. This pseudoextinction comes about since the greater parts of the two molecules of the asymmetric unit can to a good approximation be interconverted by the translation $(\vec{a}+\vec{c})/2$. 6176 independent reflections were measured with MoK_α-radiation (Nb filter) on an automatic single crystal diffractometer up to a maximum θ value of 30° (5-value measurement; $\theta/2\theta$ scan). 2109 reflections were unobserved ($I \leq 2\sigma_I$). The structure was solved by direct methods. An E-Fourier synthesis with 213 phased reflections showed the positions of the phosphorus atoms which fulfil the higher symmetry of the space group B2/b. In a subsequent Fourier synthesis with all reflections phased by the phosphorus atoms it was possible to recognize the sulfur atoms which breached the symmetry of the more highly symmetrical space group. The remaining atoms (F and N) could be located by a further Fourier synthesis with inclusion of the sulfur atoms in the phase determination. Refinement by the method of least squares, first using isotropic and then anisotropic temperature factors converged at an R value of 5.2% (observed reflections).

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The analysis showed that *(1)* does not have the proposed constitution *(1a)*[1], but that of a 9λ⁴-thia-2,4,6,8,10,11-hexaaza-1λ⁵,3λ⁵,5λ⁵,7λ⁵-tetraphosphabicyclo[5.3.1]undeca-1,3,5,7(11),8,9-hexaene *(1b)*. The bridging of the cyclotetraphosphazene system by the SN_2 group permits planar arrangement of the P—N=S=N—P system (Fig. 1). The six-membered ring arising by virtue of the SN_2 bridge proves to have a half-boat conformation with the apex at N-4. This conformation is consistent with that of the 4-(4-chlorophenyl)-4,5-dihydro-3*H*-1λ⁴,2,6-thiadiazine[3], in which the SN_2 group is likewise part of a six-membered ring.

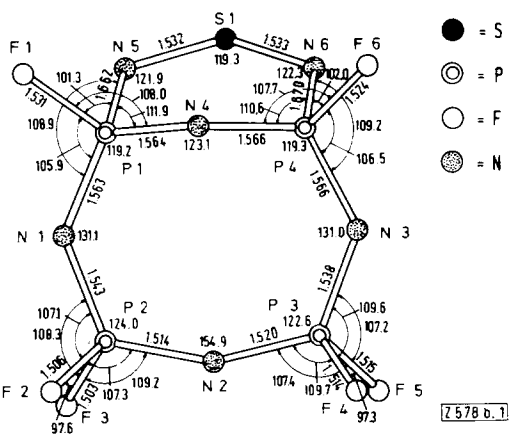

Fig. 1. Structure of the 9λ⁴-thia-2,4,6,8,10,11-hexaaza-1λ⁵,3λ⁵,5λ⁵,7λ⁵-tetraphosphabicyclo[5.3.1]undeca-1,3,5,7(11),8,9-hexaene *(1b)*. The bond lengths and angles have been averaged over the two molecules of the asymmetric unit. The mean standard deviations are 0.003 Å for the bond lengths and 0.2° for the bond angles.

The eight-membered cyclotetraphosphazene ring has a crown-saddle conformation, the larger part of which is flattened out. Except at N-4 the eight-membered ring is almost planar. The greatest deviation from planarity of the best plane through its atoms (excluding N-4) is only 0.11 Å. In the crystalline state the molecule has, to a first approximation, a plane of symmetry through S-1, N-4, and N-2 perpendicular to the best plane through the eight- and six-membered rings.

The S—N bonds are 1.53 Å long and are pure S^{IV}=N double bonds, as has also been found in all other sulfur diimides investigate by X-ray structure analysis. The angle at the sulfur atom (119.3°) is practically the same as that in 4-(4-chlorophenyl)-4,5-dihydro-3*H*-1λ⁴,2,6-thiadiazine[3]: (118.5°). The S—N bond lengths point to the fact that there is no coupling between the d_π-p_π electron system of the SN_2 group and that of the cyclotetraphosphazene ring. This fact is also supported by the P—N bond lengths. In the cyclotetraphosphazene ring the P—N bond lengths vary between 1.56 and 1.51 Å and thus evidence distinct partial double bonding, whereas the P—N bond lengths to the SN_2 system (1.67 Å) are more than 0.1 Å longer. The variation in the length of the P—N bonds in the phosphazene ring can be correlated with the degree of fluorine substitution at the phosphorus atom and the bond angles at the N atoms: the P—N bond length is shorter the higher the degree of F-substitution and the

large the bond angle at N. The bond angle at N-2 is much larger and, with a value of 154.9 , is to our knowledge the largest bond angle so far found at a formally sp^2 hybridized nitrogen atom.

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[3] *A. Gieren* and *F. Pertlik*, Angew. Chem. *88*, 852 (1976); Angew. Chem. Int. Ed. Engl. *15*, 782 (1976).

Reaction between Molybdate(VI), Cyanide, and Hydrogen Sulfide

By *Michael G. B. Drew, Philip C. H. Mitchell*, and *Christopher F. Pygall*[*]

Complexes of molybdenum with sulfide as ligand may serve as models of the binding of inorganic sulfide in molybdoenzymes, *e.g.* xanthine oxidase. We have therefore determined the structures of the complex anions *(1)*[1] and *(2)*[2] isolated from reaction of H_2S and CN^- with aqueous solutions of molybdate(VI) as their salts *(1a)* and *(2a)* by single-crystal X-ray crystallography[3]. There was also formed during the reaction a new heptacyanomolybdenate(II) anion *(3)*, which we have isolated as the potassium salt *(3a)* and structurally characterized[4]. The anion is pentagonal bipyramidal.

$Ba_3[Mo_2S_2(CN)_8] \cdot 14\ H_2O$
(1a)

$K_7[Mo_2S(CN)_{12}] \cdot 0.5\ [MoO_4]^{2-} \cdot 5\ H_2O$
(2a)

$K_5[Mo(CN)_7] \cdot 2\ H_2O$
(3a)

The structures of the anions are shown in Figure 1. In anion *(1)* the Mo_2S_2 group is planar. The Mo—S bond lengths [2.36(1) and 2.37(1) Å] are comparable with those in the well-known di-μ-sulfidomolybdenum(V) complexes[5] but the Mo—Mo distance [2.644(5) Å] is shorter and the Mo—S—Mo angles [67.9(3) and 68.3(3)°] smaller. The IR bands at 444 and 320 cm^{-1} are assigned to vibrations of the MoS_2Mo group.

In the anion *(2)* the molybdenum atoms are seven-coordinate pentagonal bipyramidal and are bridged through an axial sulfur atom. The Mo—S—Mo angle is 169.5(3)°. The Mo—S bonds [2.172(5) Å] are exceptionally short and identical within experimental error to those in $[MoS_4]^{2-}$[6]. The anion *(2)* is the first example of a molybdenum complex with a single sulfide bridge. Assignment of the IR band at 623 cm^{-1} was hitherto uncertain[2] but we can now assign it to the ν_{as}(MoSMo) vibration [we calculate ν_{as} for the MoSMo group to be *ca.* 600 cm^{-1}].

Having determined the structures of *(1)* and *(2)* and isolated the salts we can now understand the reaction between $[MoO_4]^{2-}$, H_2S, and CN^-: in the absence of oxygen reaction

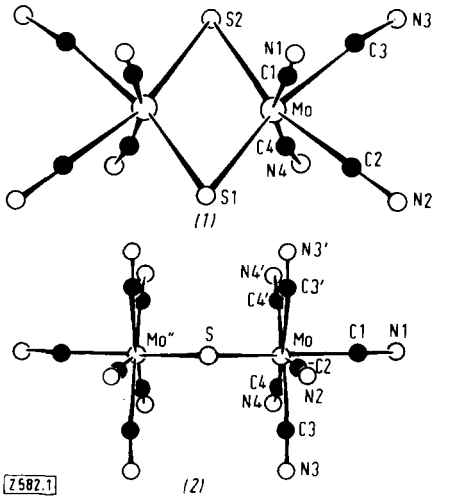
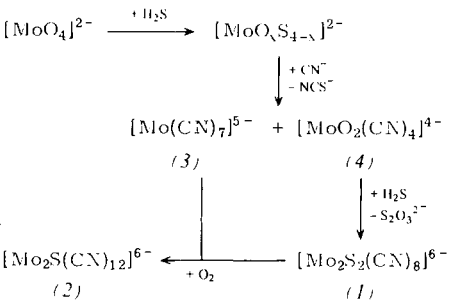


Fig. 1. Structures of anions *(1)* and *(2)*.

yields *(1)* and *(3)*, and in the presence of oxygen these products react further to give *(2)*. The anion *(4)*, already known, was an intermediate[7]. The reaction is remarkable in that molybdenum(VI) is reduced to molybdenum(II) in aqueous solution under mild conditions. Evidently cyanide stabilizes low-valent molybdenum; with oxygen- and nitrogen-donor ligands reduction below molybdenum(III) is not possible in aqueous solution.



The initial reduction of Mo^{VI} with formation of thiocyanate

$$S^{2-} + CN^- \rightarrow NCS^- + 2e^-$$

warrants interest in that a similar reaction occurs when cyanide deactivates the molybdoenzyme xanthine oxidase[8]. This observation and other evidence suggest that the "labile sulfur" of xanthine oxidase is sulfide terminally bound to molybdenum.

Procedure:

MoO_3 (7.0 g) was dissolved in water (100 ml) containing KOH (5.8 g). KCN (25.3 g) was added to this solution and the resulting solution was freed from dissolved oxygen by repeated evacuation and back-filling with N_2 in a Schlenk tube fitted with a sintered glass gas inlet. H_2S was passed through the solution for 0.5 h. The solution, after standing overnight, deposited blue crystals of $K_6[Mo_2S_2(CN)_8] \cdot 4H_2O$, which were filtered off. The filtrate, after cooling in ice, gave a mixture of yellow crystals of $K_5[Mo(CN)_7] \cdot H_2O$ and more blue crystals.

The barium salt *(1a)* was prepared by fractional crystallization from a solution containing the potassium salt and barium chloride.

Compound *(2a)* was prepared according to ref. [2] but crystals were only obtained when the molybdate impurity was not removed.

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[2] A. Müller and P. Christophliemk, Angew. Chem. 81, 752 (1969); Angew. Chem. Int. Ed. Engl. 8, 753 (1969).
[3] General Electric XRD 5 diffractometer.—(1a): 1339 independent reflections ($R=0.09$): space group $P2_1/m$; $a=8.930(6)$, $b=17.432(21)$, $c=10.029(8)$ Å; $\beta=99.3(14)°$; $Z=2$. · (2a): 1936 independent reflections ($R=0.068$): space group Pmmn; $a=15.089(10)$, $b=11.753(9)$, $c=9.113(8)$ Å; $Z=2$.
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ABSTRACTS

The use of transition metals in organic synthesis is reviewed in an article by *A. P. Kozikowski* and *H. F. Wetter*. The article is subdivided according to types of transformation. Cleavage of a functional group, as in the decarbonylation of acyl halides and aldehydes is catalyzed *e.g.* by chlorotris(triphenylphosphane)rhodium, $Fe(CO)_5$, $KHFe(CO)_4$, and $Ni(CO)_4$. Insertion reactions in the presence of $Na_2Fe(CO)_4$, $Fe(CO)_5$, or Pd^{II} enable preparation of aldehydes *etc.* from alkyl bromides, iodides, and tosylates. Transition metals activate alkene, alkyne, and allyl systems, and thus permit access to addition reactions or to introduction of functional groups. Further methods for the formation of CC bonds are iron(III) pivalate catalyzed coupling of alkyl halides with Grignard compounds and the dimerization of isoprene by a Pd^{II} system. Palladium, nickel, rhodium, and iron compounds are frequently used a catalysts in the synthesis of cyclic compounds having three to seven (and more) members. [Transition Metals in Organic Synthesis. Synthesis *1976*, 561—590; 144 references]

[Rd 897 IE—M]

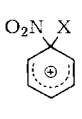
***Ipso* attack in aromatic nitration** is reported on by *R. B. Moodie* and *K. Schofield*. The following reactions take place in the presence of sulfuric or perchloric acid:

$$ArH + NO_2^{\oplus} \rightleftharpoons [ArH \cdot NO_2^{\oplus}]$$

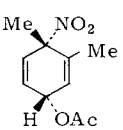
$$[ArH \cdot NO_2^{\oplus}] \rightleftharpoons \underset{NO_2}{\overset{\oplus}{Ar}\overset{H}{\diagup}} \longrightarrow ArNO_2 + H^{\oplus}$$

(1)

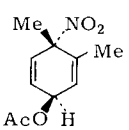
The position of the nitro group in the end product is determined during formation of the intermediate *(1)*. The ion NO_2^+ cannot only enter the ring at a position *ortho*, *meta*, or *para* to a substituent X, but also at the *ipso* position, *i.e.* at the position already bearing a substituent [cf. *(2)*]. Thus, the nitration of *o*-xylene with nitric acid/acetic anhydride



(2)



(3a)



(3b)

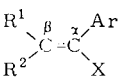
proceeds *via* the moderately stable stereoisomers *(3a)* and *(3b)*. [Ipso Attack in Aromatic Nitration. Acc. Chem. Res. *9*, 287—292 (1976); 58 references]

[Rd 898 IE—L]

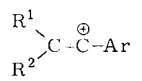
Sulfenic acid groups in proteins form the theme of a paper by *W. S. Allison*. Free SH groups in proteins can be readily oxidized *in vitro* to SOH groups. Since almost all sulfenic acids are unstable and the SOH group has no characteristic spectroscopic properties their occurrence had to be proven indirectly. If Cys-149 is present in glyceraldehyde 3-phosphate dehydrogenase in the SOH form, the enzyme does not act as dehydrogenase but as acyl phosphatase. SOH groups in general could possibly play a role in enzyme-catalyzed reactions. [Formation and Reactions of Sulfenic Acids in Proteins. Acc. Chem. Res. *9*, 293—299 (1976); 46 references]

[Rd 899 IE—L]

The solvolysis of α-arylvinyl derivatives *(1)* is described in an article by *Z. Rappoport*. The sp^2 hybridization of the vinyl carbon of a vinyl compound increases its electronegativity, strengthens the bond to the leaving group X, and infers a lower self-solvolytic reactivity for the system than for saturated systems. For compensation compounds containing highly activating substituents are employed. Bulky β-substituents have



(1)



(2)

a strong influence on the behavior of the α-arylvinyl compounds *(1)*. In many cases the solvolysis proceeds *via* free, linear, selective α-arylvinyl cations *(2)*. [Solvolysis of α-Arylvinyl Derivatives. Acc. Chem. Res. *9*, 265—273 (1976); 46 references]

[Rd 900 IE—L]

Transition-metal dialkylamides and disilylamides are dealt with in paper by *D. C. Bradley* and *M. H. Chisolm*. These compounds, *e.g.* $W(NMe_2)_6$ and $Mn[N(SiMe_3)_2(THF)$, contain transition-metal nitrogen bonds and in many cases are characterized by having unusual coordination numbers. Use of extremely bulky ligands such as $N(i\text{-}Pr)_2$ and $N(SiMe_3)_2$ has enabled isolation of complexes having coordination number two or three, *e.g.* $Cr[N(i\text{-}Pr)_2]_3$. Less bulky ligands such as NMe_2 or NEt_2 allow higher coordination numbers and in lower valency metal complexes oligomerization may occur by bridge formation between metal and ligand or by direct metal-metal bonding. An example is $Mo_2(NMe_2)_6$. [Transition-Metal Dialkylamides and Disilylamides. Acc. Chem. Res. *9*, 273—280 (1976); 108 references]

[Rd 901 IE—L]

Microbial Transformations of Non-Steroid Cyclic Compounds. By *K. Kieslich*. Georg Thieme Verlag, Stuttgart 1976. 1st edit., xxii, 1262 pp., 449 formula schemes, 225 tables, bound, DM 196.—.

The first volume of "Neuere Methoden der präparativen Organischen Chemie" (edited by *W. Foerst*) contains a section on the "Use of Biochemical Oxidation and Reduction for Preparative Purposes," in which *F. G. Fischer* describes the application of microorganisms in chemical reactions. Since this publication in the 'forties' many processes for the microbial treatment of organic compounds have been developed, so that *Klaus Kieslich* has now been able to present a very comprehensive book. Microbial steroid reactions, which have been extensively investigated, are not dealt with, since there have already been summarizing publications on this subject.

After a rather short introduction of eight pages on the methods and techniques of preparation of organic compounds with the aid of microorganisms, the possible reactions are reviewed in chapters on: 1. alicyclic compounds, 2. terpenoids, 3. aromatic compounds, 4. O-heterocycles, 5. N-heterocycles, 6. alkaloids, 7. two- and three-N heterocycles, 8. S-, O,S-, S,N- and other heterocycles, and 9. carbohydrates. The greater part of the book (826 pages) consists of a tabular presentation divided as follows: 1. oxidations, 2. reductions, 3. hydrolyses, 4. elimination of water and condensations, 5. degradations, 6. formation of new carbon-carbon or heteroatom bonds, 7. isomerizations and rearrangements. An alphabetical list of the microorganisms used is appended. The literature is covered by 1932 references up to 1973/74, with an addendum up to 1975. In a work of this scope errors and omissions are practically unavoidable. For example, in the tabulation part oxidative breakdown of aromatic compounds by bacteria is said to proceed by way of an epoxide and a *trans*-dihydrodihydroxy compound, whereas the correct interpretation with the formation of the *cis*-compound is given by the author himself on page 89.

The theme of this book can be classified as "biotechnology", a subject that is pursued in English-speaking countries and especially in Japan in accord with its importance. In West Germany much ground still has to be made up, and thus wide distribution of this book is desirable in spite of its high price.

Franz Lingens [NB 349 IE]

Experimentelle Einführung in Grundlagen und Methoden der Chemie (Experimental Introduction to the Principles and Methods of Chemistry). By *E. J. Slowinski, W. L. Masterton* and *W. C. Wolsey*. Gustav Fischer Verlag, Stuttgart 1976. 1st edit., viii, 327 pp., 18 figs., 7 flow diagrams, 10 SEM Photographs and 15 tables, paperback, DM 29.80.

The experimental chemistry book follows the trend, observed in recent years, of departing from the long-practised concept of overloading the student in his first semesters with a wealth of reading and experiments.

Here again, then, the selected material is treated by means of experiments. Several experimental procedures are presented for each theme, whether from physical, inorganic, or organic chemistry, and the selection is left to the person in charge of the class. The procedures are thoroughly worked out and are backed up by the theory needed for their understanding. The authors have further attempted, and in the reviewer's opinion successfully, to stimulate the student by questions to a critical appraisal of the apparatus and experiments and, when necessary, to extending their knowledge by referring to textbooks. The book takes the student first through the various possibilities of chemical separations and then treats the important laws of stoichiometry, calorimetry, and chemical bonding. Next come experiments on themes involving chemical equilibria, chemical kinetics, acids and bases, complex chemistry, and electrochemistry. In the remaining 80 pages the principles of qualitative analysis are presented, and here too there is no dearth of theoretical and practical explanations.

The formats and diagrams by which the student should evaluate his experimental data are well-chosen.

Thus, the book satisfies the demands that must be made on a practical chemistry text. It can be recommended without reservations for all practical work in which students are to be introduced to the methods and principles of chemistry.

Lothar Knoll [NB 350 IE]

Handbook of Organic Reagents in Inorganic Analysis. By *Z. Holzbecher, L. Diviš, M. Král, L. Šúcha*, and *F. Vláčil*. Translated by *S. Kortlý*. John Wiley & Sons, Inc., New York–London 1976. 1st edit., 734 pp., 90 figs., 90 tables, bound, $ 41.80.

According to the foreword, this book is intended as an introduction into the theory and practice of organic reagents on the grounds that up to the present there have been few monographs other than ones dealing with either of these aspects alone (which, however, is not true at least of the German and the Russian languages). However sensibly the combination is effected, the reader will, according to his standpoint, easily find something to disagree with in one or the other part. The theory is in part elementary—indeed trivial—and much of it seems superfluous. Nevertheless, some sections are very well written, for example those about absorption spectra and luminescence. The experimentalist will search in vain for a specific analytical procedure, though it must be said that it is in the practical part that the greatest value of the book will be found.

The book contains six main chapters. Following an introduction (30 pp.) the theoretical aspects are first laid down: in the second chapter (90 pp.) "Structure and Properties of Organic Reagents and their Compounds with Metals" the discussion deals with the nature of bonding in complexes, stereochemistry, isomerism, absorption spectra, luminescence, solubility, and structure. The third chapter (60 pp), "Equilibria of Organic Reagents in Solution" covers thermodynamics, kinetics, redox reactions, distribution and precipitation equilibria, and masking.

In the practical part, Chapter 4 (100 pp.) entitled "Applications of Organic Reagents in Inorganic Analysis" treats all the important analytical operations; it contains several very well written sections, particularly that on chelometric titration with an extensive table providing the choice of indicators. Chapter 5, on "Analytical Applications of Organic Reagents" (200 pp.), is probably the most important part of the book; in 50 sections and 50 tables arranged according to the periodic table it presents suitable reagents for each element from hydrogen to platinum together with keyword data for methods of determination, reaction conditions, range of determinations, and interferences. This chapter is certainly of great value to every analyst and for all who work with organic reagents. Nevertheless, the tabular presentation does not replace a real set of procedures, and one is thus referred to the original literature. Here, however, we falter, for the selection of references is incomplete. This, of course, cannot ever be completely avoided, for the author must be given the right of subjective choice, but it should never occur, as it does here, that there is no citation for many of the reagents and methods listed in

the tables. The sixth chapter (100 pp.), "Choice of Reagents Used in Analytical Chemistry", contains a collection of the formulas, names, and most important properties of organic reagents, and thus forms the requisite supplement to the preceding chapter.

The book is intended for a wide circle of readers and users, each of whom will find in it something useful and worthwhile. The student can certainly draw some gain from the very elementary theoretical chapters; users of organic reagents will use the practical chapters with success. Certain deficiencies, however, should not be overlooked.

Fritz Umland [NB 351 IE]

Laborpraxis—Quantitative Analyse. (Laboratory Practice—Quantitative Analysis.) By *W. Feler* and *C. Räthe*. Verlag Chemie, GmbH, Weinheim 1976. 1st edit., 128 pp., 21 figs., paperback, DM 12.80.

This book deals with gravimetry and mass analysis. Although the theoretical foundations of these methods are sometimes treated too skimpily, many general, useful, and valuable tips are to be found in the practical part. Procedures for some selected gravimetric determinations are described in detail, namely individual determinations of iron, nickel, aluminum, sulfate, and calcium, and separations of iron from nickel, calcium from magnesium, lead from copper. The mass-analytical part contains neutralization volumetric analysis, precipitation volumetric analysis, complexometry, and the most important procedure of redox volumetric analysis (permanganometry, chromatometry, and iodometry). Detailed experimental procedures supplement the theoretical considerations of these methods. The book is thus of interest above all to the experimentalist, *i.e.* the laboratory assistant or chemical technician, but also to the student in his first semesters.

More recent methods, such as precipitation from homogeneous solution or titration with the aid of ion-selective electrodes, are not described. On the credit side, errors are considered along with the detailed analytical directions; questions and exercises (with answers) stimulate the reader to think for himself. Unfortunately, the book suffers from a number of printing errors.

Siegbert Pantel [NB 352 IE]

Elektrochemische Bauelemente (Electrochemical Components). By *A. F. Bogenschütz* and *W. Krusemark*. Verlag Chemie GmbH, Weinheim 1976. 1st edit., x, 247 pp., 211 figs., 26 tables, bound, DM 145.—.

The coulometer, developed by *Faraday* in marketable form as early as 1840, and the electrolytic capacitor, now about 100 years old, are among the components that still hold an undisputed position in electrochemical engineering. The authors describe such perfected products but in addition do not shirk from offering many addenda and ideas for their development. Here we find the time switch (*e.g.* sea-water-activated silver/gold cells), the electrolytic information-storage devices (*e.g.* metistron and memistor), electrokinetic components (*e.g.* the solion) and electrochromic displays.

The whole book is easy for the non-expert to read, and is made easier to understand by the extremely instructive drawings and circuit diagrams. One would have liked to see more regular comparison with electronic apparatus against which these new cells must compete. Wherever ionic mobility is important for the operation of the apparatus the electronic elements must win on speed. In addition, chemical material transfer is reversible only to a limited degree, which has its effect on the life of the apparatus. A critical assessment of the prospects of specific developments should be incorporated in a new edition.

Sensors such as are used in medicine and environmental surveillance are described, as are controllers and switches, all with the same clarity noted above. Perhaps more space could be secured for this part of the book by deleting sections such as those on electrochemical thermocouples, radiation dosimeters, and coulometric determination of layer thicknesses.

The book, which construes the term "components" in a very broad sense, can be recommended both as a review and as a reference work. The 603 references provided facilitate entry into the original literature.

Ferdinand v. Sturm [NB 353 IE]

Aspects of Organic Photochemistry. By *W. M. Horspool*. Academic Press Inc., Ltd., London 1976. 1st edit., 290 pp., bound, £ 9.50.

According to the Preface, this book was written as an introduction for undergraduates and graduates facing their final examination. It is divided into nine chapters: introduction to the physical principles of photochemistry, experimental methods, the Woodward-Hoffmann rules, photochemistry of unsaturated and aromatic compounds, reactions of ketones, photochemistry of enones, oxidation and reduction reactions and finally "miscellaneous" reactions.

The main part of the book (about 200 out of its 280 pages) is devoted to preparative organic photochemistry. The author has taken great trouble to make the wealth of material easier to follow by extensive subsectioning; that this has been only partly successful is due to the involved and often inexact description of the contents.

The first chapters—"Physical Principles" and "The Woodward-Hoffmann Rules"—are inadequate as an introduction. Besides very vague statements (*e.g.* on p. 17, "Thus the molecules in the excited state are considerably more reactive in the excited state and endeavour to return to the ground state as rapidly as possible"), the text also contains a large number of serious errors which must lead to considerable confusion.

One could perhaps use this book together with others when collecting information on a specific class of reactions; however, it cannot be recommended as a beginner's introduction to the field of organic photochemistry.

Karl-Heinz Grellmann [NB 354 IE]

Solid State Photochemistry. A Collection of Papers by *G. M. J. Schmidt* and his Collaborators Describing a Symbiotic Relationship between X-Ray Crystallography and Synthetic Organic Photochemistry. Edited by *D. Ginsburg*. Monographs in Modern Chemistry, Vol. 8. Edited by *H. F. Ebel*. Verlag Chemie, Weinheim—New York 1976. 1st edit., viii, 280 pp., bound, DM 86.—.

This book, which appeared in memory of *G. M. J. Schmidt* in connection with the fifth anniversary of his death, was conceived as a report on the current state of organic solid-state chemistry which is controlled by the topology of the crystal structure in the sense of minimal change in the atomic positions, and which was called topochemistry by *Schmidt* in his capacity as its founder. The concept was extended by his student *Cohen* in the same sense. The title chosen by the editor is not really accurate, since *Schmidt* himself drew heterogeneous gas/crystal reactions into the range of his considerations and investigations. The greatest part of the book is occupied by reprints of 31 publications by *Schmidt* and his students. From these the preparative possibilities and the limits of the methods become clear; short passages by *D. Ginsburg* as editor link the various texts. The closing articles by *M. D. Cohen*, *J. D. Dunitz*, and *G. S. Hammond* treat the present, past, and future of the field. *Cohen* describes further development of research in this area at the Weizmann Institute; *Dunitz* draws

a very lively, clearcut picture of *Schmidt*, based on personal memories, and of his influence on X-ray structure determination from 1919 to 1971; *Hammond* raises the difficult question about the future of solid-state chemistry, but answers it only from the quantitative point of view.

In spite of its heterogeneity the book succeeds in providing interesting stimulation and insight even for those unfamiliar with the subject, and in this sense can be warmly recommended.

Gerhard Lehmann [NB 355 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Structure and Bonding. Edited by *J. D. Dunitz, P. Hemmerich, J. A. Ibers, C. K. Jørgensen, J. B. Neilands, D. Reinen,* and *R. J. P. Williams.* Vol. 29: Biochemistry. Springer-Verlag, Berlin 1976. iv, 219 pp., bound, DM 68.—.—ISBN 3-540-07886-X.

Rodd's Chemistry of Carbon Compounds. Edited by *S. Coffey.* Vol. I: Aliphatic Compounds. Part G: Tetrahydric Alcohols, Their Oxidation Products and Derivatives. Cumulative Index Vol. 1 Parts A—G. Elsevier Publishing Company, Amsterdam 1976. 2nd Edit., xiv, 344 pp., bound, Dfl. 115.00.—ISBN 0-444-41447-9.

Relaxation Kinetics. By *C. F. Bernasconi.* Academic Press, New York 1976. xi, 288 pp., bound, $ 29.50.—ISBN 0-12-092950-3.

Fortschritte in der Lebensmittelwissenschaft. Edited by *H. J. Bielig.* No. 4: Amine und Nitrosamine. Vorkommen, Bedeutung, Stoffwechsel und Bestimmung. By *A. Askar.* Universitätsbibliothek der TU Berlin 1976. v, 222 pp., paperback, DM 10.50.—ISBN 3-7983-0204-9.

Inorganic Aspects of Biological and Organic Chemistry. By *R. P. Hanzlik.* Academic Press, New York 1976. xvii, 402 pp., bound, $ 37.00.—ISBN 0-12-324050-6.

NMR Basic Principles and Progress/Grundlagen und Fortschritte. Edited by *P. Diehl, E. Fluck,* and *R. Kosfeld.* Vol. 12: Chlorine, Bromine and Iodine NMR. Physico-Chemical and Biological Applications. By *B. Lindman* and *S. Forsén.* Springer-Verlag, Berlin 1976. xiv, 368 pp., bound, DM 96.—.—ISBN 3-540-07725-1.

Advances in Chromatography, Vol. 14. Edited by *J. C. Giddings, E. Grushka, J. Cazes,* and *P. R. Brown.* Marcel Dekker, New York 1976. xiii, 459 pp., bound, SFrs. 114.—.—ISBN 0-8247-6436-6.

Landolt-Börnstein: Numerical Data and Functional Relationships in Science and Technology. New Series. Edited by *K.-H. Hellwege.* Group 2: Atomic and Molecular Physics. Vol. 8 (Supplement to Vol. 2): Magnetic Properties of Coordination and Organometallic Transition Metal Compounds. By *E. König* and *G. König.* Springer-Verlag, Berlin 1976. xxxvi, 1163 pp., bound, DM 1100.—.—ISBN 3-540-07441-4.

Gmelins Handbuch der Anorganischen Chemie. Main work, System No. 47: Blei. Part A: Geschichtliches. Vorkommen. 2a: Kosmochemie. Geochemie. Springer-Verlag, Berlin 1976. 8th Edit., xiv, 280 pp., bound, DM 581.—.—ISBN 3-540-93324-7.

Crystallographic Computing Techniques. Edited by *F. R. Ahmed, K. Huml,* and *B. Sedlaček.* Munksgaard, Kopenhagen 1976. 503 pp., bound, D.kr. 336.—.—Proceedings of an International Summer School Organized by The Commission on Crystallographic Computing of the International Union of Crystallography, Prague/ČSSR, July 28—August 5, 1975.—ISBN 87-16-02132-0.

Transition Metal Organometallics in Organic Synthesis, Vol. I. Edited by *H. Alper.* Vol. 33-I of the series "Organic Chemistry". Edited by *A. T. Blomquist* and *H. H. Wasserman.* Academic Press, New York 1976. ix, 258 pp., bound, $ 26.50.—ISBN 0-12-053101-1.

Proceedings of the First European Symposium on Thermal Analysis. (University of Salford, U. K., 20—24 September 1976, Organized by the Thermal Methods Group of the Analytical Division of the Chemical Society.) Edited by *D. Dollimore.* Heyden, London 1976. xxxv, 458 pp., bound, £ 11.50.—ISBN 0-85501-172-6.

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AUTHOR INDEX

G.E. = Reference to Volume *88* (1976) of the German Edition of Angewandte Chemie. References are given for Review Articles and Short Communications only.

"G.E. –" indicates an Abstract or a Book Review.

ABELES, R. H. 563
Ackermann, G. 247
Adiwidjaja, G. 40 [G.E. 25]
Ahmed, F. R. 488 [G.E. 505]
Allen, N. S. 177
Allison, W. S. 785
Almassy, R. J. 388
Alsmann, R. 769 [G.E. 809]
Alt, H. G. 759 [G.E. 800]
Anastassiou, A. G. 370 [G.E. 382]
Andersen, R. A. 609 [G.E. 692]
Andresen, A. 630 [G.E. 689]
Appel, R. 315, 696, 702 [G.E. 340, 763, 769]
Arpe, H.-J. 709
Asmus, P. 310 [G.E. 343]
Attig, R. 491 [G.E. 507]
Aumann, R. 376, 609, 610 [G.E. 375, 640, 641]
Austic, R. E. 707
Averbeck, H. 610 [G.E. 641]

BAARDMAN, F. 369 [G.E. 412]
Bachhuber, H. 385 [G.E. 386]
Bailey, P. M. 490 [G.E. 506]
Baker, D. H. 707
Balzani, V. 57
Barnett, G. H. 551 [G.E. 616]
Bartholomé, E. 448
Bartlett, P. D. 634
Bartsch, R. A. 57
Basolo, F. 245
Bauer, H. 52 [G.E. 53]
Beck, W. 495 [G.E. 511]
Beckhaus, H. 293 [G.E. 296]
Beckmann, W. 549 [G.E. 581]
Beek, W. J. 389
Behrendt, D. 544 [G.E. 608]
Beneke, K. 544 [G.E. 608]
Bergerhoff, G. 56 [G.E. 60]
Berggård, I. 507
Bergman, R. G. 232 [G.E. 254]
Berke, H. 624 [G.E. 684]
Bernal, I. 776 [G.E. 847]
Berndt, A. 698 [G.E. 764]
Bernhagen, W. 617 [G.E. 651]
Bernhard, H. O. 566
Besecke, S. 551 [G.E. 616]
Besenhard, J. O. 683 [G.E. 719]
Besl, G. 543 [G.E. 584]
Bestmann, H. J. 115, 298 [G.E. 92, 297]
Betts, F. 119
Biekert, E. 448
Biersack, H. 164 [G.E. 191]
Bingham, E. 446
Birnie, G. D. 636
Bischof, P. 556 [G.E. 609]
Blackburne, I. D. 245
Blanck, K. 488 [G.E. 505]
Blöck, E. 385 [G.E. 386]
Blomberg, C. 246
Blout, E. R. 507
Bochmann, M. 779 [G.E. 850]
Bock, H. 383, 384, 699, 700 [G.E. 380, 381, 765, 766]
Böck, H. 566
Bogenschütz, A. F. 787
Boháčková, V. 565
Böhnke, E. 499 [G.E. 512]
Boldt, P. 608 [G.E. 641]
Bolletta, F. 57
Bönnemann, H. 46 [G.E. 50]
Boss, R. 558 [G.E. 578]
Bosse, D. 557 [G.E. 610]
Bothe, E. 380 [G.E. 413]
Boulter, D. 318
Boyer, P. D. 58
Bradley, D. C. 785
Brähler, G. 699 [G.E. 765]
Braig, C. 709
Brauer, D. J. 48 [G.E. 52]
Braun, D. 451, 636 [G.E. 487, —]
Brew, K. 707
Brinen, J. S. 507
Britton, M. D. 346 [G.E. 365]
Brocker, U. 228 [G.E. 262]
Brockmann, jr., H. 115 [G.E. 93]
Brunner, H. 316, 776 [G.E. 342, 847]
Buddrus, J. 436 [G.E. 478]
Budzikiewicz, H. 58, 566
Bürvenich, C. 297 [G.E. 332]
Busse, H. G. 689 [G.E. 728]

CABANTCHIK, Z. I. 446
Calderon, N. 401 [G.E. 433]
Callaham, L. I. 247
Campbell, P. N. 176
Chance, B. 563
Chien, J. C. W. 58
Chisolm, M. H. 785
Christl, M. 493 [G.E. 508]
Clough, R. L. 543 [G.E. 584]
Collman, J. P. 177
Connolly, J. W. 700 [G.E. 766]
Connors, T. A. 176
Cooke, C. 246
Cordell, G. A. 564
Cordes, H.-G. 630 [G.E. 689]
Cottam, G. L. 749 [G.E. 821]
Cotton, F. A. 447
Couret, C. 429 [G.E. 445]
Coyle, J. D. 177
Cuatrecasas, P. 57
Cunningham, B. A. 506

DAHLENBURG, L. 110 [G.E. 127]
Dainton, F. S. 119
Dalbey, W. 446
Dannenberg, J. J. 519 [G.E. 602]
Danzer, W. 495 [G.E. 511]
Davis, J. H. 232 [G.E. 254]
Dean, J. A. 178
Debaerdemaeker, T. 504 [G.E. 544]
Deber, C. M. 507
Dederer, B. 783 [G.E. 853]
Degani, C. 58
Dehnicke, K. 553 [G.E. 612]
Dejonghe, J.-P. 371 [G.E. 417]
Delbecq, F. 496 [G.E. 537]
de Mayo, P. 506
de Meijere, A. 166, 429, 557, 686, 761 [G.E. 153, 446, 610, 721, 802]
Dennis, N. 1 [G.E. 41]
Derbyshire, E. 318
Deslauriers, R. 176
Dialer, K. 566
Diana, G. D. 410 [G.E. 458]
Dickerson, R. E. 388
Diehl, H. 104, 107, 108 [G.E. 121, 124, 125]
Dimroth, K. 238, 503 [G.E. 229, 543]
Distler, W. 298 [G.E. 297]
Divis, L. 786
Doak, G. O. 246
Dolphin, D. 563
Dornfeld, H. 633 [G.E. 691]
Drew, M. G. B. 784 [G.E. 855]
Dubois, R. 708
Dumont, W. 161 [G.E. 184]
du Mont, W.-W. 308, 308 [G.E. 303, 304]
Dvořák, J. 565
Dyong, I. 302 [G.E. 301]

EBERL, K. 554 [G.E. 575]
Eberle, G. 492, 627 [G.E. 509, 644]
Ebert, H.-D. 41 [G.E. 25]
Eckert, H. 681 [G.E. 717]
Eckert, H. G. 525 [G.E. 565]
Eckert, P. 168 [G.E. 150]
Edmonson, D. E. 507
Eglinton, G. 246
Eichenauer, H. 549 [G.E. 579]
Eigen, M. 448
Elhadi, F. E. 224 [G.E. 224]
Ely, N. 708
Enders, D. 549 [G.E. 579]
Engelhardt, H. 711
Englhardt, A. 59
Enzmann, F. 242 [G.E. 228]
Ernest, I. 207 [G.E. 244]
Ernst, J. 778 [G.E. 851]
Ernst, L. 303 [G.E. 335]
Ertel, W. 261 [G.E. 311]
Ertl, G. 391 [G.E. 423]
Escudié, J. 429 [G.E. 445]
Evans, B. 551 [G.E. 616]

FÄHNLE, M. 159 [G.E. 190]
Farnsworth, N. R. 564
Fatiadi, A. J. 446
Fehrle, M. 305 [G.E. 337]
Felcht, U. 378 [G.E. 377]
Feler, W. 787
Fennema, O. R. 709
Fenske, D. 381 [G.E. 415]
Ferrige, A. G. 223 [G.E. 223]
Fischer, E. O. 157, 231, 543, 616, 623, 683 [G.E. 163, 228, 584, 646, 683, 719]
Fischer, G. 236, 385 [G.E. 257, 386]
Fischer, H. 435 [G.E. 445]
Fitjer, L. 762, 763 [G.E. 803, 804]
Fitz, I. 565
Fitzer, E. 246
Flick, W. 309 [G.E. 305]
Flohr, H. 427, 561 [G.E. 443, 613]
Florkin, M. 178
Flues, W. 379 [G.E. 411]
Follmann, H. 499 [G.E. 512]
Försterling, H.-D. 449
Forth, W. 121
Frank, A. 157, 231, 234, 433, 612, 623, 632, 682, 701 [G.E. 163, 228, 255, 450, 648, 683, 649, 719, 768]
Frank, W. 686 [G.E. 760]
Freedman, L. D. 246
Freitag, G. 493 [G.E. 508]
Frensch, K. 685 [G.E. 722]
Friedrich, K. 261 [G.E. 311]
Friedrich, P. 701 [G.E. 768]
Frigon, R. P. 707
Fritz, E. 246
Fritz, G. 699 [G.E. 765]
Fuchs, J. 374, 375 [G.E. 385, 385]
Fuhrhop, J.-H. 551, 648, 778 [G.E. 616, 704, 851]
Full, R. 45 [G.E. 55]
Füller, H.-J. 501 [G.E. 541]
Funk, R. L. 53 [G.E. 63]

GÄB, S. 433 [G.E. 479]
Galante, Y. 176
Galver, A. J. 609 [G.E. 692]
Gässer, O. 502 [G.E. 542]
Geiss, K.-H. 437 [G.E. 449]
Gensler, A. 365 [G.E. 374]
Gerson, F. 552 [G.E. 617]
Ghosez, L. 371 [G.E. 417]
Gieren, A. 760, 782, 783 [G.E. 802, 852, 853]
Giese, B. 173, 174, 237, 688 [G.E. 159, 161, 258, 723]
Giesecke, H. 169 [G.E. 151]
Gilette, J. R. 507
Gillespie, R. J. 318
Glässel, W. 701 [G.E. 768]
Gleisberg, D. 354 [G.E. 354]
Glemser, O. 614 [G.E. 646]
Gompper, R. 299, 301, 321 [G.E. 298, 300, 389]
Gore, J. 496 [G.E. 537]
Gossauer, A. 626 [G.E. 642]
Grate, J. H. 170 [G.E. 186]
Grätzel, M. 633 [G.E. 690]
Griesbaum, K. 55 [G.E. 59]
Griffith, W. P. 120

Griller, D. 317
Grimme, W. 53 [G.E. 63]
Grob, C. A. 569 [G.E. 621]
Gröger, C. 373 [G.E. 415]
Grund, H. 50 [G.E. 27]
Grund, N. 242 [G.E. 228]
Gunstone, F. D. 317
Günzler, H. 566
Gupta, D. 508
Gutmann, V. 319

HADERT, H. 711
Hafner, K. 104, 107, 108, 314 [G.E. 121, 124, 125, 341]
Halevi, E. A. 593 [G.E. 664]
Hall, L. D. 119
Hall, W. K. 57
Hallensleben, M. L. 163 [G.E. 192]
Halstenberg, M. 696 [G.E. 763]
Hamann, C. H. 447
Hammer, R. 42, 612 [G.E. 61, 648]
Hamprecht, B. 194 [G.E. 211]
Hamza, A. 226 [G.E. 226]
Hanstein, W. G. 176
Häring, H. W. 386 [G.E. 383]
Harmon, H. J. 563
Harnisch, H. 468 [G.E. 517]
Harper, H. A. 710
Harris, K. R. 634
Harris, R. K. 389
Harris, R. L. N. 498 [G.E. 539]
Hartan, H.-G. 226 [G.E. 252]
Hartl, H. 375 [G.E. 385]
Hartmann, G. R. 181 [G.E. 197]
Harto, S. 40 [G.E. 25]
Hartz, P. 354 [G.E. 354]
Hatefi, Y. 176
Häusler, J. 497 [G.E. 538]
Havsteen, B. 689 [G.E. 728]
Heger, K. 53 [G.E. 62]
Hehre, W. J. 177
Heidmann, W. 546, 547 [G.E. 576, 577]
Heimann, M. 367 [G.E. 376]
Heimbach, P. 49 [G.E. 29]
Hekman, M. 431 [G.E. 447]
Helfand, E. 176
Hellmann, H. 448
Helmchen, G. 703 [G.E. 770]
Helmreich, E. J. M. 318
Hemmerich, P. 443 [G.E. 475]
Hengesbach, J. 433 [G.E. 450]
Hengge, E. 319, 370 [G.E. —, 414]
Henglein, A. 633 [G.E. 690]
Henne, A. 435 [G.E. 445]
Henrici-Olivé, G. 136 [G.E. 144]
Henschler, D. 121
Herberhold, M. 230, 366, 617 [G.E. 227, 375, 651]
Herberich, G. E. 433 [G.E. 450]
Herrmann, W. A. 164, 368, 615, 695 [G.E. 191, 379, 652, 761]
Herwig, J. 630 [G.E. 689]
Heublein, G. 566
Heumann, K. G. 55 [G.E. 54]
Hevesi, L. 381 [G.E. 413]
Himbert, G. 51 [G.E. 59]
Hirsch, W. 626 [G.E. 642]
Ho, T.-L. 774 [G.E. 847]
Hoberg, H. 694 [G.E. 760]
Hocker, J. 169 [G.E. 151]
Hoffman, B. M. 245
Hoffmann, R. 55 [G.E. 54]
Höfle, G. 113 [G.E. 89]
Hollenberg, M. D. 57
Hollitzer, O. 444 [G.E. 480]
Holzbecher, Z. 786
Holzer, N. 624 [G.E. 685]
Holzinger, W. 702 [G.E. 768]
Hopf, H. 165, 628 [G.E. 152, 687]
Horn, H. 297 [G.E. 332]
Hornemann, U. 109 [G.E. 87]
Horowitz, N. H. 245
Horspool, W. M. 787
Horton, E. W. 245
House, H. O. 446
Hrdina, P. D. 446
Hudson, M. F. 119
Hugelin, B. 49 [G.E. 29]
Huppatz, J. L. 498 [G.E. 539]
Huttner, G. 157, 231, 234, 433, 495, 612, 623, 632, 682, 701 [G.E. 163, 228, 255, 450, 511, 648, 683, 649, 719, 768]

IBERS, J. A. 245
Ingledew, W. J. 563
Ingold, K. U. 317
Ippen, J. 613 [G.E. 643]
Irngartinger, H. 562 [G.E. 615]
Isaacs, N. S. 564
Isenhour, T. L. 178
Ishihara, T. 611 [G.E. 650]
Itahara, T. 160 [G.E. 154]

JACKMAN, L. M. 447
Jacob, E. 158, 159 [G.E. 189, 190]
Jäger, H.-U. 562 [G.E. 615]
Jäger, V. 50 [G.E. 27]
Janda, M. 443 [G.E. 475]
Jander, J. 225 [G.E. 225]
Janning, J. 660 [G.E. 737]
Jansen, M. 376 [G.E. 410]
Janssen, E. 39, 783 [G.E. 24, 853]
Jennings, H. J. 176
Jersch, N. 302 [G.E. 301]
Jessen, W. 689 [G.E. 728]
Johnson, W. S. 9 [G.E. 33]
Johnston, H. S. 176
Jonas, K. 47, 621, 622, 767 [G.E. 51, 682, 682, 808]
Jost, K. H. 565
Jostkleigrewe, E. 779 [G.E. 812]
Judy, W. A. 401 [G.E. 433]
Jugelt, W. 246
Jurs, P. C. 178
Jutzi, P. 295, 684 [G.E. 333, 720]

KAI, Y. 297 [G.E. 295]
Kaim, W. 700 [G.E. 766]
Kalbacher, H. 297 [G.E. 332]
Kalchschmid, F. 773 [G.E. 849]
Kalder, H.-J. 623 [G.E. 683]
Kalinowski, H. O. 234 [G.E. 256]
Kaminsky, W. 629, 630, 660 [G.E. 688, 689, 737]
Kammermeyer, K. 247
Kämper, F. 306 [G.E. 334]
Kandler, J. 354 [G.E. 354]
Kasai, N. 297 [G.E. 295]
Kaschig, J. 305 [G.E. 337]
Katada, T. 766 [G.E. 844]
Kato, S. 766 [G.E. 844]
Katritzky, A. R. 1, 245 [G.E. 41, —]
Katz, R. N. 170, 542 [G.E. 186, 583]
Kauffmann, Th. 500 [G.E. 513]
Kaupp, G. 163, 441, 442, 779 [G.E. 185, 482, 482, 812]
Kawamura, K. 611 [G.E. 650]
Kayama, Y. 487 [G.E. 536]
Kemmer, T. 115 [G.E. 93]
Kempe, U. M. 427 [G.E. 443]
Kern, A. 625 [G.E. 686]
Kieslich, K. 786
Kinast, G. 239 [G.E. 261]
Kinberger, K. 434, 779 [G.E. 451, 850]
Kipnis, D. M. 57
Kirmse, W. 251 [G.E. 273]
Kisielowski, L. 298 [G.E. 297]
Kitahara, Y. 487 [G.E. 536]
Kitschke, B. 106 [G.E. 123]
Kläui, W. 172 [G.E. 187]
Klein, H.-F. 42, 612 [G.E. 61, 648]
Kleine, W. 616 [G.E. 646]
Klessinger, M. 310 [G.E. 343]
Klingebiel, U. 312, 313, 619 [G.E. 307, 304, 647]
Klug, H.-H. 229 [G.E. 268]
Knackmuss, H.-J. 549 [G.E. 581]
Knauf, P. 446
Knoll, F. 315, 702 [G.E. 340, 769]
Knollmann, R. 302 [G.E. 301]
Knözinger, E. 25 [G.E. 1]
Koberstein, E. 586 [G.E. 657]
Koch, D. 160 [G.E. 154]
Koebernick, W. 439 [G.E. 477]
Köhler, F. H. 554, 623 [G.E. 575, 683]
Kolář, C. 440 [G.E. 478]
Kölle, U. 433 [G.E. 450]
Königer-Ahlborn, E. 680 [G.E. 725]
Kopf, J. 629, 768 [G.E. 688, 811]
Korte, F. 120, 433 [G.E. —, 479]
Koryta, J. 565
Köster, H. 546, 547 [G.E. 576, 577]
Kouwenhoven, A. P. 369 [G.E. 412]
Kozikowski, A. P. 785
Kraemer, H. P. 243 [G.E. 230]
Kral, M. 786
Kramolowsky, R. 768 [G.E. 811]
Krannich, H.-J. 110, 311 [G.E. 88, 338]
Krapcho, A. P. 635
Krause, S. 694 [G.E. 760]
Krebs, B. 39, 633 [G.E. 28, 691]
Kreher, R. 382 [G.E. 419]
Kreissl, F. R. 157, 231, 543, 616, 632 [G.E. 163, 228, 584, 646, 649]
Kresze, G. 760 [G.E. 801]
Kricheldorf, H. R. 305 [G.E. 337]
Krief, A. 161, 381 [G.E. 184, 413]
Kröher, R. 692 [G.E. 758]
Kröhnke, F. 245
Krolikiewicz, K. 689 [G.E. 724]
Krüger, C. 46, 48, 609, 621, 767, 779 [G.E. 50, 52, 640, 682, 808, 850]
Krusemark, W. 787
Küchler, E. 533 [G.E. 555]
Kunau, W.-H. 61 [G.E. 97]
Kutschan, R. 626 [G.E. 642]
Kutzelnigg, W. 390
Kuwajima, I. 498 [G.E. 539]

L'ABBE, G. 489 [G.E. 510]
Labhart, H. 708
Labinger, J. A. 333 [G.E. 402]
Lagaly, G. 544, 575 [G.E. 608, 628]
Lange, B. 113 [G.E. 89]
Lardy, H. 177
Laszlo, P. 707
Laurence, G. S. 57
Lea, P. J. 564
Lee, J. C. 797
Lehninger, A. L. 318
Lehr, F. 505 [G.E. 540]
Leithe, W. 58
Leitich, J. 372 [G.E. 416]
Lenck, R. 768 [G.E. 811]
Leonhard, K. 230 [G.E. 227]
Lesiecki, H. 41 [G.E. 25]
Levsen, K. 509 [G.E. 589]
Ley, H. 448
Lin, C.-H. C. 177
Lindner, E. 41 [G.E. 25]
Lindner, H. J. 106 [G.E. 123]
Lindner, T. L. 157, 231, 632 [G.E. 163, 228, 649]
Lindoy, L. F. 120
Litscher, G. 370 [G.E. 414]
Liu, A. T. 495 [G.E. 511]
Liu, B. Y. H. 710
Lloyd, D. 459 [G.E. 496]
Löffler, G. 710
Lommel, H. 59
Löwe, A. 566
Lübbecke, H. 608 [G.E. 641]
Luber, J. 111 [G.E. 91]
Lübke, K. 741 [G.E. 790]
Lubosch, W. 313 [G.E. 339]
Lückoff, M. 503 [G.E. 543]
Luftmann, H. 306 [G.E. 334]
Lukas, J. H. 369 [G.E. 412]

MADISON, V. 507
Mahjour, S. 374 [G.E. 385]
Maier, G. 226 [G.E. 252]
Mairanovsky, V. G. 281 [G.E. 283]
Maitlis, P. M. 490, 507 [G.E. 506, —]
Malisch, W. 618, 769 [G.E. 680, 809]
Malissa, H. 141 [G.E. 168]
Mandelkern, L. 447
Manfrin, M. F. 57
Märkl, G. 690 [G.E. 728]
Marquarding, D. 627 [G.E. 644]
Marr, G. 246
Martin, H.-D. 431 [G.E. 447]
Masterton, W. L. 786
Matern, E. 699 [G.E. 765]
Mathieu, J. 179
Matsuura, T. 160 [G.E. 154]
Mattausch, H. 624 [G.E. 685]
Mattes, R. 118 [G.E. 92]
Maurer, H. 628 [G.E. 687]

Mayer, E. 773 [G.E. 849]
Mayer, K. K. 164 [G.E. 191]
Mayring, L. 554 [G.E. 575]
McKellar, J. F. 177
McNab, H. 459 [G.E. 496]
Meier, H. 117, 380 [G.E. 94, 413]
Meier, W. 508
Meissner, U. E. 365 [G.E. 374]
Meller, A. 312, 313, 619 [G.E. 307, 304, 647]
Menig, H. 702 [G.E. 768]
Menke, K. 165 [G.E. 152]
Mennemann, K. 118 [G.E. 92]
Merali, Z. 446
Merck, A. 630 [G.E. 689]
Merritt, Jr., L. L. 178
Merten, R. 169 [G.E. 151]
Mews, R. 614, 691 [G.E. 646, 757]
Meyer, N. 438 [G.E. 484]
Meyer, W. 499 [G.E. 512]
Meyers, A. I. 270 [G.E. 321]
Midgley, D. 177
Miflin, B. J. 564
Mihelich, E. D. 270 [G.E. 321]
Mills, R. 634
Minard, R. D. 164 [G.E. 191]
Mislow, K. 317
Mitchell, P. C. H. 784 [G.E. 855]
Mitchell, P. R. 548 [G.E. 585]
Miyazaki, H. 487 [G.E. 536]
Mizuta, M. 766 [G.E. 844]
Möbius, H.-H. 247
Moggi, L. 57
Mohmand, S. 383 [G.E. 380]
Mohr, G. 682 [G.E. 719]
Möller, H. 382 [G.E. 419]
Moodie, R. B. 785
Mösinger, O. 103 [G.E. 120]
Moss, J. R. 269
Mottweiler, R. 630 [G.E. 689]
Mühlhausen, D. 307 [G.E. 338]
Mukaiyama, T. 94 [G.E. 111]
Müller, A. 633, 680 [G.E. 691, 725]
Müller, H. 620 [G.E. 681]
Müller, J. 702 [G.E. 768]
Mulliken, R. S. 246
Murata, I. 240, 297, 611 [G.E. 262, 295, 650]
Muschiol, M. 776 [G.E. 847]
Musso, H. 373 [G.E. 415]
Muttzall, K. M. K. 389
Mynott, R. 767 [G.E. 808]

NÄDER, R. 166 [G.E. 153]
Naegele, D. 764 [G.E. 805]
Nakamura, E. 498 [G.E. 539]
Nakasuji, K. 611 [G.E. 650]
Narita, M. 635
Nast, R. 110 [G.E. 127]
Nau, H. 75 [G.E. 74]
Neidlein, R. 775 [G.E. 810]
Neudert, B. 308, 308 [G.E. 303, 304]
Nichols, D. G. 318
Niecke, E. 309, 692 [G.E. 305, 758]
Niemeier, R. 446
Nishinaga, A. 160 [G.E. 154]
Nitsch, H. 760 [G.E. 801]
Nitz, S. 433 [G.E. 479]
Normant, J. F. 371 [G.E. 417]
Nöth, H. 235 [G.E. 231]

ODA, M. 487 [G.E. 536]
Oesterhelt, D. 17, 187 [G.E. 16, 203]
Ofstead, E. A. 401 [G.E. 433]
Öhler, E. 42 [G.E. 54]
Ohya-Nishiguchi, H. 552 [G.E. 617]
Ōki, M. 87 [G.E. 67]
Olafsson, S. N. 768 [G.E. 811]
Olah, G. A. 446, 774 [G.E. —, 847]
Olivé, S. 136 [G.E. 144]
Ollis, W. D. 223, 224, 757 [G.E. 223, 224, 798]
Opferkuch, R. 158 [G.E. 190]
Orama, O. 234 [G.E. 255]
Osowska, K. 302 [G.E. 302]
Otter, R. 500 [G.E. 513]
Otting, W. 52, 549 [G.E. 53, 581]

PADBERG, H.-J. 56 [G.E. 60]
Padwa, A. 123 [G.E. 131]
Pancic, F. 410 [G.E. 458]
Panico, R. 179
Pannhorst, W. 427, 561 [G.E. 443, 613]
Panster, P. 618 [G.E. 680]
Park, S.-W. 494 [G.E. 511]
Parlar, H. 433 [G.E. 479]
Patterson, J. M. 563
Paulat, V. 39 [G.E. 28]
Paulat-Böschen, I. 633 [G.E. 691]
Paulsen, H. 438, 439, 440 [G.E. 476, 477, 478]
Pein, J. 630 [G.E. 689]
Permutt, M. A. 57
Pertlik, F. 782 [G.E. 852]
Pestemer, M. 179
Peter, H. 49 [G.E. 29]
Peter, W. 43 [G.E. 26]
Petrides, R. E. 710
Pfeiffer, G. 52 [G.E. 53]
Pfletschinger, J. 428 [G.E. 444]
Phillips, J. N. 498 [G.E. 539]
Pickardt, J. 374 [G.E. 385]
Pierrard, C. 43 [G.E. 26]
Pietrzik, E. 297 [G.E. 332]
Pittmann, Jr., C. U. 635
Platonov, V. B. 634
Plettenberg, H. 436 [G.E. 478]
Plieninger, H. 243 [G.E. 230]
Pohl, S. 162, 309, 687 [G.E. 162, 305, 723]
Pohmakotr, M. 437 [G.E. 449]
Poisel, H. 294 [G.E. 295]
Pörschke, K. R. 621 [G.E. 682]
Portier, J. 475 [G.E. 524]
Posner, A. S. 119
Powell, J. T. 707
Pressler, W. 112 [G.E. 88]
Prinzbach, H. 559 [G.E. 611]
Pritzkow, H. 225, 771 [G.E. 225, 846]
Proksch, E. 761 [G.E. 802]
Pustoslemsek, P. 704 [G.E. 771]
Pygall, C. F. 784 [G.E. 855]

QUAST, H. 168 [G.E. 150]
Quick, A. 757 [G.E. 798]

RÄTHE, C. 787
Rampal, J. B. 690 [G.E. 728]
Rappoport, Z. 785
Rau, H. 114 [G.E. 90]
Redhouse, A. D. 615 [G.E. 652]
Redoulès, G. 429 [G.E. 445]
Reed, P. 177
Reetz, M. T. 705 [G.E. 726]
Regitz, M. 378 [G.E. 377]
Rehn, D. 627 [G.E. 644]
Rehn, H. 627 [G.E. 644]
Reichardt, C. 112 [G.E. 88]
Reichmanis, E. 370 [G.E. 382]
Reisner, M. G. 776 [G.E. 847]
Reitmeier, H. 187 [G.E. 203]
Renger, B. 234 [G.E. 256]
Renk, T. 779 [G.E. 850]
Rétey, J. 427, 561 [G.E. 443, 613]
Retzlaff, G. 389
Richarz, W. 108 [G.E. 125]
Ried, W. 103, 494, 704 [G.E. 120, 511, 771]
Rieker, A. 160 [G.E. 154]
Rieser, J. 261 [G.E. 311]
Ringsdorf, H. 764 [G.E. 805]
Roberts, P. J. 48 [G.E. 52]
Rockett, B. W. 246
Roden, K. 439 [G.E. 477]
Rodier, J. 319
Roesky, H. W. 39, 226, 693, 783 [G.E. 24, 226, 759, 853]
Rogers, D. 757 [G.E. 798]
Roloff, A. 49 [G.E. 29]
Rösch, K. 163 [G.E. 185]
Rösch, L. 620 [G.E. 681]
Rosmus, P. 383, 384 [G.E. 380, 381]
Rothe, M. 307, 770 [G.E. 338, 844]
Rothstein, A. 446
Rott, H. 770 [G.E. 844]
Rücker, C. 559 [G.E. 611]
Rudolph, G. 308 [G.E. 303]
Rummel, W. 121
Rust, G. 389
Rye, R. R. 177

SANDER, V. 244 [G.E. 259]
Sandmeier, D. 115 [G.E. 92]
Sandow, T. 772 [G.E. 854]
Satgé, J. 429 [G.E. 445]
Saunders Jr., E. H. 317
Sawitzki, G. 552 [G.E. 616]
Sayrac, T. 226 [G.E. 252]
Schäfer, H. 713 [G.E. 775]
Schäfer, R. 613 [G.E. 643]
Schäfer, H. J. 306 [G.E. 334]
Schäfer-Ridder, M. 228, 229 [G.E. 262, 268]
Schaffer, O. 238 [G.E. 229]
Scharf, H.-D. 682 [G.E. 718]
Schaumann, E. 40 [G.E. 25]
Scheerer, R. 633 [G.E. 690]
Scheffold, R. 558 [G.E. 578]
Scherer, O. J. 379, 701, 722 [G.E. 411, 768, 845]
Schieda, O. 386 [G.E. 383]
Schieferstein, L. 622 [G.E. 682]
Schildknecht, H. 214, 242 [G.E. 235, 228]
Schillinger, E. 741 [G.E. 790]
Schluge, M. 683 [G.E. 719]
Schlupp, K. F. 341 [G.E. 348]
Schmid, G. 115 [G.E. 92]
Schmid, H.-G. 234 [G.E. 255]
Schmidbaur, H. 367, 501, 502, 728 [G.E. 376, 541, 542, 830]
Schmidpeter, A. 111, 488, 781 [G.E. 91, 505, 851]
Schmidt, A. H. 704 [G.E. 771]
Schmidt, G. M. J. 787
Schmidt, K.-D. 614 [G.E. 646]
Schmidt, R. R. 171 [G.E. 193]
Schmidt, U. 42, 294, 497 [G.E. 54, 295, 538]
Schmierer, R. 703 [G.E. 770]
Schnabl, G. 772 [G.E. 845]
Schneider, H.-J. 544 [G.E. 608]
Schofield, K. 785
Schöler, H. 702 [G.E. 769]
Schöllkopf, U. 293 [G.E. 296]
Schomburg, D. 781 [G.E. 851]
Schrader, B. 508
Schrauzer, G. N. 170, 417, 542 [G.E. 186, 465, 583]
Schreiner, K. 698 [G.E. 764]
Schubert, U. 612, 632 [G.E. 648, 649]
Schuckmann, W. 103, 494 [G.E. 120, 511]
Schulte-Frohlinde, D. 380 [G.E. 413]
Schultze, W. 711
Schulz, R. C. 777 [G.E. 848]
Schumann, H. 308, 308 [G.E. 303, 304]
Schurig, V. 304 [G.E. 336]
Schuster, O. 114 [G.E. 90]
Schutte, C. J. H. 635
Schuttenberg, H. 777 [G.E. 848]
Schwartz, J. 333 [G.E. 402]
Schwarz, H. 509, 705 [G.E. 589, 726]
Seebach, D. 234, 313, 437, 438, 505 [G.E. 256, 339, 449, 484, 540]
Seel, H. 775 [G.E. 810]
Seewald, A. 444 [G.E. 480]
Seff, K. 564
Seifert, W. J. 238 [G.E. 229]
Seiter, W. 55 [G.E. 59]
Sekutowski, J. C. 767 [G.E. 808]
Seppelt, K. 44, 377, 766, 771 [G.E. 56, 410, 806, 846]
Seufert, A. 295 [G.E. 333]
Sharpe, A. G. 709
Shea, K. J. 232 [G.E. 254]
Sheldrick, W. S. 115, 778, 781 [G.E. 93, 851, 851]
Shibata, S. 673 [G.E. 750]
Sidiropoulos, G. 693 [G.E. 759]
Siebels, H.-J. 760 [G.E. 802]
Siebert, W. 45, 434, 779 [G.E. 55, 451, 850]
Sigel, H. 548 [G.E. 585]
Simchen, G. 428 [G.E. 444]
Simon, A. 624 [G.E. 685]
Singer, T. P. 507
Singhal, R. L. 446
Singleton, E. 246
Sinn, H. 629, 630, 660 [G.E. 688, 689, 737]
Sinnwell, V. 438, 439 [G.E. 476, 477]
Skell, P. S. 695 [G.E. 761]
Slowinski, E. J. 786
Smith, I. C. P. 176
Smith, K. M. 119, 551 [G.E. —, 616]
Solouki, B. 383, 384 [G.E. 380, 381]
Sommer, S. 432 [G.E. 449]
Somorjai, G. A. 635

Sondheimer, F. 117 [G.E. 126]
Spielmann, W. 429 [G.E. 446]
Srivastava, S. C. 109 [G.E. 87]
Staab, H. A. 365 [G.E. 374]
Stahl, E. 389
Steckhan, E. 294 [G.E. 306]
Steglich, W. 444 [G.E. 480]
Steiner, W. 684 [G.E. 720]
Stellmach, J. 237 [G.E. 258]
Stenzel, W. 440 [G.E. 478]
Stephanatou, J. S. 223, 757 [G.E. 223, 798]
Stetter, H. 639, 686 [G.E. 695, 760]
Steudel, R. 772 [G.E. 854]
Stiggall, D. L. 176
Stoddart, J. F. 223, 224, 757 [G.E. 223, 224, 798]
Stoessl, A. 564
Stokes, B. O. 58
Storch, W. 235 [G.E. 231]
Stothers, J. B. 564
Stotz, E. H. 178
Sturm, L. 545 [G.E. 574]
Sucha, L. 786
Suda, M. 314 [G.E. 341]
Sumper, M. 187 [G.E. 203]
Sundermeyer, W. 110, 311 [G.E. 88, 338]
Suschke, H. D. 247
Süss, G. 366 [G.E. 375]
Süss, H. U. 104 [G.E. 121]
Swinbourne, E. S. 247

TAKEUCHI, Y. 1, 245 [G.E. 41, —]
Talbiersky, J. 171 [G.E. 193]
Tanimoto, S. 613 [G.E. 648]
Tatsuoka, T. 297 [G.E. 295]
Thewalt, U. 765 [G.E. 807]
Tieke, B. 764 [G.E. 805]
Thieme, H. K. 261 [G.E. 311]
Thompson, S. J. 490 [G.E. 506]
Tietze, L.-F. 239 [G.E. 261]
Timasheff, S. N. 707
Timkovich, R. 388
Toffel, P. 633 [G.E. 690]
Töpert, M. 741 [G.E. 790]
Troxler, E. 49 [G.E. 29]
Tsay, Y.-H. 46, 48, 621, 767 [G.E. 50, 52, 682, 808]
Tsutsui, M. 708

UGI, I. 492, 627, 681 [G.E. 509, 644, 717]
Ulrich, H. 354 [G.E. 354]
Ulrich, W.-R. 299, 301 [G.E. 298, 300]
Urban, R. 627 [G.E. 644]

VASISHT, S. K. 236 [G.E. 257]
Vaska, L. 707
Veith, M. 387, 696 [G.E. 384, 762]
Veltmann, H. 315 [G.E. 340]
Verhelst, G. 489 [G.E. 510]
Vickrey, T. M. 170, 542 [G.E. 186, 583]
Vielstich, W. 447
Vieweg, R. 636
Villieras, J. 371 [G.E. 417]
Vlacil, F. 786
Voelter, W. 297 [G.E. 332]
Vogel, E. 228, 229, 613 [G.E. 262, 268, 643]
Vogler, A. 625 [G.E. 686]
Vögtle, F. 685 [G.E. 722]
Voigt, E. 117 [G.E. 94]
Vollhardt, K. P. C. 53 [G.E. 63]
Vollmer, H.-J. 629, 630 [G.E. 688, 689]
von Schnering, H. G. 552 [G.E. 616]
von Sonntag, C. 380 [G.E. 413]
Vorbrüggen, H. 689 [G.E. 724]

WACHTER, J. 316 [G.E. 342]
Wagner, H.-U. 321 [G.E. 389]
Wagner, P. H. 382 [G.E. 419]
Wagner-Jauregg, T. 564
Waibel, J. 389
Walker, E. R. H. 389
Wallenfels, K. 261 [G.E. 311]
Wang, S.-T. 247
Ward, E. W. B. 564
Waterman, M. R. 749 [G.E. 821]
Weast, R. C. 178
Wegner, G. 764 [G.E. 805]
Weidenbruch, M. 43 [G.E. 26]
Weidenhammer, K. 164, 368, 695 [G.E. 191, 379, 761]
Weigert, W. M. 448, 586 [G.E. —, 657]
Weill-Raynal, J. 179
Weinmaier, J. H. 781 [G.E. 851]
Weiss, J. 379 [G.E. 411]
Weissberger, E. 707
Weissermel, K. 709
Weisz, H. 150 [G.E. 177]
Weitemeyer, C. 686 [G.E. 721]
Wellmann, J. 294 [G.E. 306]
Welz, B. 447
Wentworth, R. A. D. 388
Werner, G. 247
Werner, H. 172 [G.E. 187]
Wetter, H. F. 785
Weyerstahl, P. 244 [G.E. 259]
White, C. 490 [G.E. 506]
Wiaux-Zamar, C. 371 [G.E. 417]
Wiberg, N. 236, 385, 386 [G.E. 257, 386, 383]
Wien, H. 341 [G.E. 348]
Wihler, H.-D. 702 [G.E. 769]
Wikström, M. K. H. 563
Wilkinson, G. 609 [G.E. 692]
Willard, H. H. 178
Williams, D. J. 757 [G.E. 798]
Williams, J. M. 491 [G.E. 507]
Wilz, I. 242 [G.E. 228]
Winkler, R. 448
Winston, A. E. 370 [G.E. 382]
Winter, W. 241 [G.E. 260]
Wolcott, R. G. 58
Wolmershäuser, G. 379 [G.E. 411]
Wolsey, W. C. 786
Wolters, E. 682 [G.E. 718]
Wong, H. N. C. 117 [G.E. 126]
Wörmann, H. 609 [G.E. 640]
Wood, H. G. 707
Wright, D. J. 318
Wurm, H. 163 [G.E. 192]
Würthwein, E.-U. 112 [G.E. 88]
Wydler, C. 552 [G.E. 617]

YAKOBSON, G. G. 634
Yamamoto, K. 240 [G.E. 262]
Yasuoka, N. 297 [G.E. 295]
Yoffe, A. D. 446

ZEINER, H. 695 [G.E. 761]
Zeiss, W. 555 [G.E. 582]
Ziegler, M. L. 162, 164, 242, 368, 695 [G.E. 188, 191, 228, 379, 761]
Zimmermann, H.-E. 507
Zimmermann, I. 441 [G.E. 482]
Zipprich, M. 225 [G.E. 225]
Zöller, M. 162 [G.E. 188]
Zwierzak, A. 302 [G.E. 302]
Zymalkowski, F. 120

SUBJECT INDEX

FP = Full paper (review article) LA = Literature abstract
SC = Short communication
G.E. = Reference to Volume *88* (1976) of the German Edition of Angewandte Chemie.
References are given for Review Articles and Short Communications only.

ABSOLUTE configuration, The ~ of 2-(2,4,5,7-tetranitro-9-fluorenylideneaminooxy)propionic acid (TAPA) (SC) 115 [G.E. 93]
Determination of the ~ of chiral thiols by ^{1}H-NMR spectroscopy of diastereomeric thiol esters (SC) 703 [G.E. 770]
Structure and ~ of an organo-iron compound having iron as chiral center (SC) 776 [G.E. 847]
Aceheptylene, Cycloadditions of ~. Facile synthesis of dicyclopenta[ef,kl]heptalenes (SC) 108 [G.E. 125]
Acetic acid derivatives, Reaction of N-protected succinimides with α-lithiated ~ (SC) 626 [G.E. 642]
Acetylenes, Fluoride catalyzed addition of silyl-~ to carbonyl compounds (SC) 498 [G.E. 539]
The photochemical addition of acetylene to tricarbonyl(η^5-cyclopentadienyl)methylmolybdenum and -tungsten (SC) 759 [G.E. 800]
Polymerization of tricosa-10,12-diynoic acid in multilayers (SC) 764 [G.E. 805]
Palladium(II)-induced oligomerization (LA)
Acylation, Nucleophilic ~ with β-acylenamines (SC) 171 [G.E. 193]
4,6-Diphenylthieno[3,4-d][1,3]dioxol-2-one 5,5-dioxide, a novel activating agent for peptide syntheses (SC) 444 [G.E. 480]
β-Acyl enamines, Nucleophilic acylation with ~ (SC) 171 [G.E. 193]
Adipose tissue, Bioenergetics of mitochondria in brown ~ (LA) 318
Air analysis, Die Analyse der Luft und ihre Verunreinigungen in der freien Atmosphäre und am Arbeitsplatz (Book Review) 58
Aldehydes, Catalyzed addition of ~ to activated double bonds—a new synthetic approach (FP) 639 [G.E. 695]
Alkaloids, Plant constituents with potential anticancer and cytotoxic activity (LA) 564
Alkenes, [2+2]-cycloaddition of alkynes to ~ (SC) 369 [G.E. 412]
Alkylation-cycloaddition, Electrophilic ~ between an olefinic and an acetylenic substrate (SC) 55 [G.E. 59]
Alkylidenemalondialdehyde, Synthesis of ~ tetramethyl bisacetals (SC) 113 [G.E. 88]
Alkynes, Electrophilic alkylation-cycloaddition between an olefinic and an acetylenic substrate (SC) 55 [G.E. 59]
[2+2]-Cycloaddition to alkenes (SC) 369 [G.E. 412]
Allenes, Trialkyl-~ from 1,1-disubstituted propargylic acetates (SC) 496 [G.E. 537]
Allopolarization, Concept of ~. Effects of substituents on reactions of ambifunctional anions (FP) 321 [G.E. 389]
Allylation of 4-hydroxyarsenin—arsenic-carbon hetero-Cope rearrangement (SC) 690 [G.E. 728]
Allyl ethers, Cleavage with Pd/C (SC) 558 [G.E. 578]
Aluminum chloride, Formation of carbenium ions in the reaction of ~ with tert-butylchloride in liquid hydrogen chloride (SC) 773 [G.E. 849]
Aluminum compounds, The Al—Al bond as a readily accessible structural unit in organometallic compounds (SC) 694 [G.E. 760]
1,3,2λ^3,4-Diazaphosphoniaaluminatacyclobutane: A cyclic zwitterion having twofold coordinated phosphorus (SC) 692 [G.E. 758]
Ambifunctional anions, Concept of allopolarization. Effects of substituents on reactions of ~ (FP) 321 [G.E. 389]
Amide cleavage, A methylenedi-λ^5-phosphazene by ~ of tetramethylphosphonium salts (SC) 501 [G.E. 541]
Amides, Transition-metal dialkyl-~ and disilyl-~ (LA) 785
Amination, Oxidative ~ of toluhydroquinone (SC) 109 [G.E. 87]
Amines, Stereospecific synthesis of β-bromo-~ by ionic addition of diethyl dibromophosphoramidate to a double bond (SC) 302 [G.E. 302]
Trifluoroacetylation of ~ with N-trifluoroacetyl-Nylon 66 (SC) 777 [G.E. 848]
Amino acids, Synthesis of α,β-dehydro esters of ~ and N-tert-butoxycarbonyl α,β-dehydro ~ (SC) 294 [G.E. 295]
Macrocyclic peptides in anionic polymers of amino acid N-carboxylic anhydrides (SC) 307 [G.E. 338]
Radical oxidation of amino acid derivatives (SC) 497 [G.E. 538]
Aminoalkylation, New variant of the Mannich reaction (SC) 239 [G.E. 261]
Nucleophilic ~. Lithiated N,N-dimethylthiopivalamide (SC) 313 [G.E. 339]
Amino groups, Phosphorus(III) derivative with sterically fixed bis(trimethylsilyl)-~ (SC) 309 [G.E. 305]
Analysis, Instrumental Methods of ~ (Book Review) 178
Handbook of organic reagents in inorganic ~ (Book Review) 786
Laborpraxis—Quantitative Analyse (Book Review) 787
Analytical methods, Far-infrared Fourier spectroscopy as a method for structure determination in chemistry (FP) 25 [G.E. 1]
Integrated dust analysis (FP) 141 [G.E. 168]
Application of catalyzed reactions in analytical chemistry (FP) 150 [G.E. 177]
Collisional activation mass spectrometry—a new probe for determining the structure of ions in the gas phase (FP) 509 [G.E. 589]
Radioimmunoassay (FP) 525 [G.E. 565]
Dual-wavelength spectrophotometry (FP) 673 [G.E. 750]
Anhydrides, Macrocyclic peptides in anionic polymers of amino acid N-carboxylic ~ (SC) 307 [G.E. 338]
4',5'-Anhydroadenosine, Detection as the cleavage product of coenzyme B_{12} in functional holoenzymes (SC) 542 [G.E. 583]
Anthranilates, Self-condensation of β-dialkylaminocrotonates: a one-step synthesis of N,N-dialkyl-~ (SC) 498 [G.E. 539]
Antibiotics, Antibiotic inhibition of mitochondrial ATP synthesis (LA) 177
Antimony complexes, Tris[dicarbonyl(η-cyclopentadienyl)ferrio]stibane—A 5B-element base with total transition-metal substitution (S) 618 [G.E. 680]
Arginine, The interrelationship between ~, glutamic acid and proline in metabolism and nutrition (LA) 707
Arsenic compounds, Synthesis and structure of a hexaazadiphosphadiarsatricyclodecane (SC) 701 [G.E. 768]
Arsenic oxide trichloride, $AsOCl_3$ (SC) 766 [G.E. 806]
Arsenic pentachloride, $AsCl_5$ (SC) 377 [G.E. 410]
Arsenin, Allylation of 4-hydroxy-~—arsenic-carbon hetero-Cope rearrangement (SC) 690 [G.E. 728]
"Arsenobenzene", C_6H_5—As=As—C_6H_5, as a bridging μ_3 ligand in a transition metal complex (SC) 234 [G.E. 255]
Asymmetric synthesis of α-substituted ketones by metalation and alkylation of chiral hydrazones (SC) 549 [G.E. 579]
Atomic absorption spectroscopy, Atom-Absorption-Spektroskopie (Book Review) 447
Atomic structure, Lehrprogramm Atombau und Periodensystem (Book Review) 709
Automotive exhaust detoxification with multifunctional catalysts (FP) 586 [G.E. 657]
9-Azabarbaralane, Unsubstituted ~: A π-destabilized heterocycle (SC) 370 [G.E. 382]
2-Azetidinones, Synthesis of β-lactams (LA) 564
9-Azidotriptycenes, Photolysis (SC) 168 [G.E. 150]
Azines, Catalytic synthesis of 1,2-diaza-1,5,9-cyclododecatrienes from butadiene and ~ (SC) 49 [G.E. 29]
Reactions of ~ and imines with dienophiles (LA) 564
Azobenzene, Carbonylchromium complexes of ~ (SC) 230 [G.E. 227]
Azo compounds, Competing cycloadditions in the reaction of acetylazobenzene with diphenylketene (SC) 432 [G.E. 449]
Azulene, Cycloadditions of pentalene and ~—A facile heptalene synthesis (SC) 104 [G.E. 121]

BACTERIORHODOPSIN, ~ as an example of a light-driven proton pump (FP) 17 [G.E. 16]
Biosynthesis of the purple membrane of halobacteria (FP) 187 [G.E. 203]
Barriers to rotation, Unusually high ~ involving the tetrahedral carbon atom (FP) 87 [G.E. 67]
Benzene, Mechanism of the thermal conversion of 3,3'-bicyclopropenyls into ~ derivatives (SC) 232 [G.E. 254]
Continuous electrocatalytic synthesis of phenol from ~ and hydrogen peroxide (SC) 294 [G.E. 306]
Indirect determination of the half-wave reduction potentials of ~ and [2.2]paracyclophane (SC) 552 [G.E. 617]
Benzo[14]annulene (SC) 365 [G.E. 374]
Benzothiepin, Low-temperature X-ray structure analysis of 1-~ (SC) 297 [G.E. 295]
New synthetic entry to the thiepin system.—Benzo[d]thiepin and dibenzo[bd]thiepin (SC) 611 [G.E. 650]
Betaines, Synthetic applications of heteroaromatic ~ with six-membered rings (FP) 1 [G.E. 41]
Bicyclo[4.2.0]octa-2,4-dienes, Photoisomerization and photocleavage of ~ (SC) 779 [G.E. 812]
Bicyclopentane, A CH carbene complex of iron by metal-induced fragmentation of two bonds of a ~ unit (SC) 609 [G.E. 640]
Oxidative addition of the central bond of a ~ system to iron (SC) 610 [G.E. 641]
3,3'-Bicyclopropenyl, Mechanism of the thermal conversion of ~-s into benzene derivatives (SC) 232 [G.E. 254]
Bicyclopropyl, Interaction of the Walsh orbitals in ~ (SC) 310 [G.E. 343]
Bile pigments (LR) 119
Bimolecular films, Kink-block and gauche-block structures of ~ (FP) 575 [G.E. 628]
Biochemistry, Comprehensive ~ (Book Review) 178
Biochemie (Book Review) 318
Biomimetic polyene cyclizations (FP) 9 [G.E. 33]
Bond angle distortion, Extreme ~ in organozirconium compounds active toward ethylene (SC) 629 [G.E. 688]
Bond order, Correlation between the β-effect of methyl groups on $\delta(^{13}C)$ and the C_α—C_β

π-~ (SC) 303 [G.E. 335]
Bones, Synthetic amorphous calcium phosphate (LR) 119
Boranes, Simple synthesis of cyclopentadienyl-~ (SC) 295 [G.E. 333]
Borolan-1-ylamine, Tris(3-methylborolan-1-yl)amine, an electron-deficient triborylamine (SC) 235 [G.E. 231]
Borole, Novel type of triple-decker complex—~ as bridging ligand (SC) 433 [G.E. 450]
Boron compounds, (1,2-Diaza-3,6-dibora-4-cyclohexene)tricarbonylchromium—A complex with an η^6-$C_2B_2N_2$ ligand (SC) 45 [G.E. 55]
Bridgehead derivatives, Optically active ~ of trishomobarrelene and trishomobullvalene (SC) 429 [G.E. 446]
Bromate, Chemical waves in the 2,4-pentanedione/potassium ~ system (SC) 689 [G.E. 728]
β-Bromoamines, Stereospecific synthesis by ionic addition of diethyl dibromophosphoramidate to a double bond (SC) 302 [G.E. 302]
Bromyl cation, $[BrO_2]$ (SC) 158 [G.E. 189]
Bullvalene, $C_{12}H_{10}O$ and thermolabile $C_{11}H_{10}O$ ketones from ~ via carbonyliron complexes (SC) 376 [G.E. 375]
Butadiene, Catalytic synthesis of 1,2-diaza-1,5,9-cyclododecatrienes from ~ and azines (SC) 49 [G.E. 29]
tert-Butyl chloride, Formation of carbenium ions in the reaction of aluminum chloride with ~ in liquid hydrogen chloride (SC) 773 [G.E. 849]

CADMIUM, Biochemical aspects of the toxicology of ~ (LA) 446
Cadmium compounds, Bis(tri-tert-butylsilyl)-cadmium: The first silylcadmium compound isolated in substance (SC) 620 [G.E. 681]
Calcium phosphate, Synthetic amorphous ~ (LA) 119
Cancer, Drugs used in treatment (LA) 176
Carbanion complexes of nickel (SC) 621 [G.E. 682]
Carbene complexes, Dimethylcarbene- and methylphenylcarbenedicarbonyl(η-cyclopentadienyl)manganese (SC) 543 [G.E. 584]
CH ~ of iron by metal-induced fragmentation of two bonds of a bicyclopentane unit (SC) 609 [G.E. 640]
Pentacarbonyl(diethylaminofluorocarbene)chromium (SC) 616 [G.E. 646]
3-Dimethylamino-3-phenylallenylidene. A novel ligand at the pentacarbonylchromium and -tungsten skeleton (SC) 623 [G.E. 683]
Simple synthesis of dicarbonyl(η-cyclopentadienyl)-(3,3-di-tert-butylallenylidene)-manganese (SC) 624 [G.E. 684]
Carbenium ions, Formation of ~ in the reaction of aluminum chloride with tert-butyl-chloride in liquid hydrogen chloride (SC) 773 [G.E. 849]
Carbocations, Theoretical approaches to the structure of ~ (LA) 177
Carbonate ion, Polarogram and reactions of a short-lived oxidation product of ~ (SC) 633 [G.E. 690]
Carbonyl compounds, Synthesis of olefins from α-silyl carbanions and ~ (SC) 161 [G.E. 184]
α-Hydroxycarboxamides from N,N-bis-(methoxymethyl)carbamoyllithium and ~ (SC) 293 [G.E. 296]
Fluoride-catalyzed addition of silylacetylenes to ~ (SC) 498 [G.E. 539]
Carboxamides, α-Hydroxy-~ from N,N-bis-(methoxymethyl)carbamoyllithium and carbonyl compounds (SC) 293 [G.E. 296]
Carboxylic acids, Regioselective chlorination of centered methylene groups in di-~ (SC) 306 [G.E. 334]
Carbyne complex, trans-Pentacarbonylrhenio-(phenylcarbyne)tetracarbonylmolybdenum: A transition metal ~ containing a metal-metal bond (SC) 157 [G.E. 163]
μ-Bromo-μ-phenylmethylidynebis(tetracarbonylrhenium) (SC) 231 [G.E. 228]
Tetrakis(trimethylsilylmethyl)bis(μ-trimethylsilylmethylidyne)ditungsten (SC) 609 [G.E. 692]
trans-Bromo(tetracarbonyl)ferrocenylcarbyne-tungsten (SC) 683 [G.E. 719]
Catalysts, ESCA investigations on industrial ~ (LA) 507
Catalyzed reactions, Application in analytical chemistry (FP) 150 [G.E. 177]
C—C Linkage of polyfunctional molecules by nucleophilic addition of dianions. Synthesis of pillarose (SC) 439 [G.E. 477]
Chelate ligand, 2,2''-Bis(diphenylphosphino)-2',3',5',6'-tetraphenyl-p-terphenyl as an arene ~ for rhodium(I) (SC) 241 [G.E. 260]
Chemical waves in the 2,4-pentanedione potassium bromate system (SC) 689 [G.E. 728]
Chemotherapy of virus diseases (FP) 410 [G.E. 458]
Chimeras of enzymes, Exchange in vitro of subunits between enzymes from different organisms: ~ (FP) 181 [G.E. 197]
Chloride complexes, Gaseous ~ with halogen bridges—homo-complexes and hetero-complexes (FP) 713 [G.E. 775]
Chlorination, Regioselective ~ of centered methylene groups in dicarboxylic acids (SC) 306 [G.E. 334]
Nonpollutative ~ and chlorinating oxidation of phenols (SC) 608 [G.E. 641]
Chlorine isotope effects in ion exchange chromatography (SC) 55 [G.E. 54]
Chlorophosphane, First example of a ~-phosphanylium chloride transformation. 2-Methyl-1,2,3λ^2-diazaphosphole hydrochlorides (SC) 111 [G.E. 91]
Chromatography, Advances in thin-layer ~ (LA) 389
Hochdruck-Flüssigkeits-Chromatographie (Book Review) 711
Chromium, π-Complexes of λ^5-phosphorins with tricarbonyl-~, tricarbonylmolybdenum, or tricarbonyltungsten (SC) 503 [G.E. 543]
Chromium complexes, (1,2-Diaza-3,6-dibora-4-cyclohexene)tricarbonylchromium—A complex with an η^6-$C_2B_2N_2$ ligand (SC) 45 [G.E. 55]
Carbonyl-~ of azobenzene (SC) 230 [G.E. 227]
"Arsenobenzene", C_6H_5—As=As—C_6H_5, as a bridging μ_3 ligand in a transition metal complex (SC) 234 [G.E. 255]
X-ray structure analysis of two π-complexes of λ^5-phosphorins with tricarbonylchromium (SC) 504 [G.E. 544]
Pentacarbonyl(diethylaminofluorocarbene)chromium (SC) 616 [G.E. 646]
Reactions of arenetricarbonyl-~ with nitrosyl chloride (SC) 617 [G.E. 651]
3-Dimethylamino-3-phenylallenylidene. A novel ligand at the pentacarbonylchromium and -tungsten skeleton (SC) 623 [G.E. 683]
Functional transition-metal phosphanes (SC) 769 [G.E. 809]
Coal, Production of oil by hydrogenation of ~ (FP) 341 [G.E. 348]
Cobaloximes, New developments in the field of vitamin B_{12}: Reactions of the cobalt atom in corrins and in vitamin B_{12} model compounds (FP) 417 [G.E. 465]
Synthesis and structure determination of an intramolecularly alkylated bridged cobaloxime (SC) 427 [G.E. 443]
Cobalt complexes, Synthesis of phosphorus ylides at a ~ center (SC) 42 [G.E. 61]
A lithium-cobalt bimetal complex (SC) 46 [G.E. 50]
Tetracarbonylcobaltiopentacarbonylmanganiomercury, $(CO)_4Co$—Hg—$Mn(CO)_5$ (SC) 162 [G.E. 188]
A mononuclear paramagnetic biphosphinotricarbonylcobalt(0) complex (SC) 381 [G.E. 415]
A novel hetero-bimetallic dinitrogen complex (SC) 612 [G.E. 648]
Cobalt compounds, New developments in the field of vitamin B_{12}: Reactions of the cobalt atom in corrins and in vitamin B_{12} model compounds (FP) 417 [G.E. 465]
Synthesis, structure determination, and rearrangement of a model for the active site of methylmalonyl-CoA mutase with incorporated substrate (SC) 561 [G.E. 613]
Bis(η-1,5-cyclooctadiene)cobaltlithium (SC) 767 [G.E. 808]
Cobalt(I)-Phthalocyanine, A new technique of protecting groups—cleavage of β-halogenated alkyl esters with supernucleophilic ~ (SC) 681 [G.E. 717]
Coenzyme B_{12}, Photochemical induction of enzymatic activity of a carbocyclic analog of ~: a contribution to the elucidation of the mechanism of action of ~ (SC) 170 [G.E. 186]
Synthesis and structure determination of an intramolecularly alkylated bridged cobaloxime (SC) 427 [G.E. 443]
Detection of 4',5'-anhydroadenosine as the cleavage product of ~ in functional holoenzymes (SC) 542 [G.E. 583]
Vitamin B_{12} coenzyme (LA) 563
Collagen, Structure and properties (LA) 58
Color Lexicon, BAG Farben-Lexikon (Book Review) 711
Complexation chromatography, Separation of deuteriated ethylenes $C_2H_{4-n}D_n$ by ~ on a rhodium(I) complex (SC) 304 [G.E. 336]
Complexes, Gaseous chloride ~ with halogen bridges—homo-~ and hetero-~ (FP) 713 [G.E. 775]
Synthesis of trinuclear sandwich-like cyclopentadienyl ~ containing two different metal atom centers (SC) 172 [G.E. 187]
Use of the isoselectivity principle for distinguishing cationic π- and σ ~ (SC) 237 [G.E. 258]
Complex formation with tetraazacycloalkane-N,N',N'',N'''-tetraacetic acids as a function of ring size (SC) 686 [G.E. 760]
Transition metal ~ of synthetic macrocyclic ligands (LA) 120
Alkali-metal ~ in aqueous solution (LA) 177
Condensation, Oxidation-reduction ~ (FP) 94 [G.E. 111]
Conformation, The conformational behavior of 5,10,11,12-tetrahydrodibenzo[a,d]cyclooctene (SC) 224 [G.E. 224]
~-s and N-inversion barriers in tropane compounds (SC) 545 [G.E. 574]
Conformational studies on twelve-membered cyclic heterocycles. Crystal structure of 5,18-dimethyl-5,18-diazatribenzo[a,e,i]-cyclododecene-6,17(5H,18H)-dione (SC) 757 [G.E. 798]
^{13}C-NMR spectroscopy and the determination of the ~-s of biological molecules (LA) 176
~ of piperidine (LA) 245
Use of cyclic peptides for conformational studies (LA) 507
Conformational diastereoisomers, Isolation of ~ of N,N',N''-tribenzyltrianthranilide (SC) 223
Cope rearrangement, ~ with dipolar intermediates (SC) 299 [G.E. 298]
Hetero ~-s with dipolar intermediates (SC) 301 [G.E. 300]
Copper compounds, S_4N_4 bridge ligand: structure of $CuCl \cdot S_4N_4$ (SC) 765 [G.E. 807]
Additions of lithium organocuprates as models for electron-transfer processes (LA) 446
Crosslinking, Penetration and ~ of macromolecules (FP) 451 [G.E. 487]
Crotonates, Self-condensation of β-dialkylamino-~: a one-step synthesis of N,N-dialkylanthranilates (SC) 498 [G.E. 539]
Crown ethers, Papaverine ~ (SC) 685 [G.E. 722]
Crystal face dependence of the surface chemistry of tungsten (LA) 177
Crystal surfaces, Reactions on surfaces of single crystals (LA) 635
Crystals and long-chain molecules (LA) 447
Cyanides of metals from the 4th—7th subgroups (LA) 120
Cyano complexes, The chemistry of ~ of the transition metals (Book Review) 709
Cyclizations, Biomimetic polyene ~ (FP) 9 [G.E. 33]
Cycloadditions, Synthetic applications of heteroaromatic betaines with six-membered

rings (FP) 1 [G.E. 41]
Intramolecular 1,3-dipolar ~ (FP) 123 [G.E. 131]
Competing ~ in the reaction of acetylazobenzene with diphenylketene (SC) 432 [G.E. 449]
Cyclobutadiene—A square singlet molecule? (SC) 226 [G.E. 252]
Cyclobutane, 1,3,2λ³,4-diazaphosphoniaaluminata-~: A cyclic zwitterion having twofold coordinated phosphorus (SC) 692 [G.E. 758]
Cyclobutane rings, Four linearly annelated ~: the tetracyclo[4.4.0.0^{2,5}.0^{7,10}]decane system (SC) 431 [G.E. 447]
Cyclobuta[b]triphenylene, 10,11-Dihydro-~ and 1,2,5,6,9,10-hexahydrotriscyclobuta[b,h,n]triphenylene (SC) 53 [G.E. 63]
Cyclobuteneselenones, Bond-delocalized ~ (SC) 704 [G.E. 771]
Cyclodiaza-λ⁶-thiane, A new cyclic SN compound: 1,1,3,3-tetraoxo-2,4-difluorosulfonyl-~ (SC) 614 [G.E. 646]
Cycloheptatsulfur oxide, Synthesis of ~, S_7O (SC) 772 [G.E. 854]
Cyclooctadiene, Cyclohexenyl(1,5-~)iridium —η-diene hydride or enyl structure (SC) 702 [G.E. 768]
Bis(η-1,5-~)cobaltlithium (SC) 767 [G.E. 808]
Cyclooctatriene, 5,8-Bis(diphenylmethylene)-1,3,6-~ (SC) 487 [G.E. 536]
5,8-Bis(7-cycloheptatrienylidene)-1,3,6-~ (SC) 487 [G.E. 536]
2,4-Cyclopentadienones, Synthesis of 3-aryl-2,5-di-tert-butyl-~ by base-catalyzed oxygenation of 4-aryl-2,6-di-tert-butylphenols (SC) 160 [G.E. 154]
Cyclopentadienylboranes, Simple synthesis (SC) 295 [G.E. 333]
Cyclopentadienyl complexes, Synthesis of trinuclear sandwich-like ~ containing two different metal atom centers (SC) 172 [G.E. 187]
Cyclopent[cd]azulene, 1,4-Dipolar cycloadditions (SC) 107 [G.E. 124]
[2.2]Cyclophanes, [6+6]Photocleavage (SC) 442 [G.E. 482]
Cyclophosphazene spanned by a sulfur diimido group (SC) 39 [G.E. 24]
1H-Cyclopropa[a]naphthalene from 2,3-benzo-1,6-methano[10]annulene (SC) 613 [G.E. 643]
Cyclopropanation of [2.2]paracyclophanes (SC) 165 [G.E. 152]
Cyclopropane rearrangement, Degenerate butadienyl-~ in tricyclo[5.3.0.0^{2,10}]deca-3,5-diene (SC) 53 [G.E. 63]
Cyclopropanes, Interaction of the Walsh orbitals in bicyclopropyl (SC) 310 [G.E. 343]
Selective hydrogenations of 1,1-disubstituted ~ (SC) 373 [G.E. 415]
Coupling reactions of vinylidenedi-~ doubly halogenated in allylic positions—a productive synthesis of trispiro[2.0.2.0.2.0]nonane ([3]rotane) (SC) 762 [G.E. 803]
1-Cyclopropene-1-carboxylates from 1-chloro-1-cyclopropanecarboxylic acids (SC) 244 [G.E. 259]
Cyclopropenyl, Electronic structure of tri-tert-butyl-~ (SC) 698 [G.E. 764]
Cyclopropyl hydrocarbons, Oxidation of ~ with ozone (SC) 761 [G.E. 802]
Cyclotetraphosphazene, The structure of a ~ spanned by a sulfur diimido group (SC) 783 [G.E. 853]
Cysteine, Optical induction during biomimetic formation of ~ (SC) 42 [G.E. 54]
Cytochrome c oxidase, Spectral, potentiometric, and energy-linked properties of ~ in mitochondria (LA) 563

5-DEAZARIBOFLAVIN and 5-thiariboflavins: a simple pathway to antimetabolites of vitamin B_2 (SC) 443 [G.E. 475]
α,β-Dehydro amino acids, Synthesis of esters of ~ and N-tert-butoxycarbonyl ~ (SC) 294 [G.E. 295]
Detoxification of automotive exhaust gases with multifunctional catalysts (Fp) 586 [G.E. 657]
Deuterioethylenes, Separation of ~ $C_2H_{4-n}D_n$ by complexation chromatography on a rhodium(I) complex (SC) 304 [G.E. 336]
1,3-Diarsacyclobutanes (SC) 56 [G.E. 60]
1,2-Diaza-1,5,9-cyclododecatrienes, Catalytic synthesis from butadiene and azines (SC) 49 [G.E. 29]
Diazadiphosphetidines, Isolation of a diaza-λ³,λ⁵- and a thermodynamically unstable diaza-λ⁵,λ⁵-diphosphetidine (SC) 555 [G.E. 582]
Synthesis and isolation of cis- and trans-1,3,2λ³,4λ³-diazadiphosphetidine (SC) 772 [G.E. 845]
Diaza[7]helicene, Simple synthesis and resolution (SC) 114 [G.E. 90]
1,2,3λ²-Diazaphosphole, First example of a chlorophosphane phosphanylium chloride transformation: 2-methyl-~ hydrochlorides (SC) 111 [G.E. 91]
5,18-Diazatribenzo[a,e,i]cyclododecene-6,17(5H,18H)-dione, Conformational studies on twelve-membered cyclic heterocycles. Crystal structure of ~ (SC) 757 [G.E. 798]
Diazene, Existence of isomeric ~-s (diimines) (SC) 385 [G.E. 386]
Bis(trimethylsilyl)-~ as a complex ligand (SC) 386 [G.E. 383]
Structure of an "isodiimine" complex: bis-(trimethylsilyl)iso-~-bis(cyclopentadienyl)-vanadium (SC) 387 [G.E. 384]
Diazoalkane, Nitrogen transfer from a ~ to a metal center (SC) 695 [G.E. 761]
Diazo compounds, μ-Methanediazo(N,N,N')-tris(tetracarbonylmanganese) (SC) 368 [G.E. 379]
Diazomethane, $Mn_2(CO)_{10}CH_2N_2$, a stable organometallic derivative of ~ (SC) 164 [G.E. 191]
Diazonium ions, Nitrogen as leaving group: aliphatic ~ (FP) 251 [G.E. 273]
Dibenzo[a,d]cyclooctene, Conformational behavior of 5,10,11,12-tetrahydro-~ (SC) 224 [G.E. 224]
Dibenzo[bd]thiepin, New synthetic entry to the thiepin system.—Benzo[d]thiepin and ~ (SC) 611 [G.E. 650]
Dictionary, Russian-English chemical and polytechnical ~ (Book Review) 247
Dicyclopenta[ef, kl]heptalenes, Cycloadditions of aceheptylene. Facile synthesis of ~ (SC) 108 [G.E. 125]
Diels-Alder reaction, Partial asymmetric ~ with an α-chloronitroso compound (SC) 760 [G.E. 801]
Diffusion, Influence of isotopic substitution on ~ in liquids (LA) 634
Diimine, Bis(trimethylgermyl)-~ (SC) 236 [G.E. 257]
Existence of isomeric diazenes (~-s) (SC) 385 [G.E. 386]
Bis(trimethylsilyl)diazene as a complex ligand (SC) 386 [G.E. 383]
Structure of an "isodiimine" complex: bis(trimethylsilyl)isodiazenebis(cyclopentadienyl)vanadium (SC) 387 [G.E. 384]
1,3,2-Dioxazolidines by thermal 1,3-cycloaddition of nitro groups to strained olefins (SC) 372 [G.E. 416]
1,2-Dioxetanes (LA) 634
1,3-Dioxolane derivatives, Synthesis of furan derivatives from 4-benzoyloxy-1,3-~ (SC) 682 [G.E. 718]
Diphenylmethyl groups, Magnetic nonequivalence of the C atoms of prochiral ~ in ^{13}C-NMR spectroscopy (SC) 234 [G.E. 256]
1,3-Dipolar cycloadditions, Intramolecular ~ (FP) 123 [G.E. 131]
Disaccharides, Synthesis of α-glycosidically linked ~ of D-galactosamine (SC) 440 [G.E. 478]
Double bonds, Catalyzed addition of aldehydes to activated ~—a new synthetic approach (FP) 639 [G.E. 695]
Drug metabolism, Environmental factors (LA) 507
Drugs used in treatment of cancer (LA) 176
Dual-wavelength spectrophotometry (FP) 673 [G.E. 750]
Dust analysis, Integrated ~ by physical methods (FP) 141 [G.E. 168]

ELECTROCATALYTIC synthesis, Continuous ~ of phenol from benzene and hydrogen peroxide (SC) 294 [G.E. 306]
Electrochemical components, Elektrochemische Bauelemente (Book Review) 787
Electrochemistry, A new electrochemical method of forming SiSi bonds (SC) 370 [G.E. 414]
Elektrolytgleichgewichte und Elektrochemie (Book Review) 247
Elektrochemie (Book Review) 447
Lehrbuch der Elektrochemie (Book Review) 565
Electro-deprotection—electrochemical removal of protecting groups (SC) 281 [G.E. 283]
Electron, The ~ as a chemical entity (LA) 119
Electron density distribution, Structure and density distribution of bonding electrons of cumulenes (SC) 562 [G.E. 615]
f-Elements, σ-Bonded organic derivatives of ~ (LA) 708
Eliminations, Association of ions in base-promoted β-~ (LA) 57
Distinction between concerted and nonconcerted ~ (LA) 317
Enamines, α-Metalated ~ (SC) 371 [G.E. 417]
Enantioselective reactions, Enantioselective Wagner-Meerwein rearrangement in chiral solvents under high pressure (SC) 243 [G.E. 230]
Energy metabolism, Evolution of bacterial ~ (LA) 388
Energy transductions, Coupling of "high-energy" phosphate bonds to ~ (LA) 58
Enkephalin, Total synthesis of methionine-~ (SC) 297 [G.E. 332]
Enols from Norrish type II cleavage of carbonyl compounds in solution (SC) 435 [G.E. 445]
Environmental chemistry Vol. 1. (Book Review) 246
Enzymes, Exchange in vitro of subunits between ~ from different organisms: chimeras of ~ (FP) 181 [G.E. 197]
Reaction mechanism of ~ containing molybdenum (LA) 388
Eschenmoser sulfide contraction, C-substitution of nucleosides with the aid of the ~ (SC) 689 [G.E. 724]
ESR spectroscopy, Electronic structure of tri-tert-butylcyclopropenyl (SC) 698 [G.E. 764]
Radical cation and radical anion of a tetrasilyl-substituted ethylene (SC) 699 [G.E. 765]
Radical cations of tetrasilyl-substituted hydrazines (SC) 700 [G.E. 766]
Esters, Catalyzed addition of aldehydes to activated double bonds—new synthetic approach (FP) 639 [G.E. 695]
Ether cleavage, Cleavage of allyl ethers with Pd/C (SC) 558 [G.E. 578]
Electron impact induced ~ by anchimeric participation of silyl and germyl groups (SC) 705 [G.E. 726]
Cleavage of esters and ethers with iodotrimethylsilane (SC) 774 [G.E. 847]
Ethylene, Separation of deuteriated ~-s $C_2H_{4-n}D_n$ by complexation chromatography on a rhodium(I) complex (SC) 304 [G.E. 336]
Extreme bond angle distortion in organozirconium compounds active toward ~ (SC) 629 [G.E. 688]
Halogen-free soluble Ziegler catalysts for polymerization of ~. Control of molecular weight by choice of temperature (SC) 630 [G.E. 689]
Ethylene complexes, Ethylenebis(phenylsodium)nickel (SC) 47 [G.E. 51]
Structure of a bimetal-~: $[(C_6H_5)_2NiC_2H_4]_2Na_4(THF)_5$ (SC) 48 [G.E. 52]
Eutrophication and wastewater purification (FP) 354 [G.E. 354]

Evolution, Genetics and biological ~ (LA) 707
Excited states, Chemistry of electronically ~ of coordination compounds (LA) 57
Exhaust gases, Detoxification of automotive ~ with multifunctional catalysts (FP) 586 [G.E. 657]
Experimental chemistry, Experimentelle Einführung in Grundlagen und Methoden der Chemie (Book Review) 786

FAR-INFRARED Fourier spectroscopy as a method for structure determination in chemistry (FP) 25 [G.E. 1]
Fatty acids, Chemistry and biochemistry of unsaturated ~ (FP) 61 [G.E. 97]
Some new chemical properties of unsaturated C_{18} acids (LA) 317
α-Ferrocenylalkylamines, Recovery of chiral ~ on stereoselective peptide synthesis by four-component condensation (SC) 492 [G.E. 509]
Field desorption mass spectrometry, Li^+-attachment—a soft ionization method in ~ (SC) 696 [G.E. 762]
Fine Particles (Book Review) 710
Fischer-Tropsch synthesis: molecular weight distribution of primary products and reaction mechanism (FP) 136 [G.E. 144]
Flavins, 8α-Substituted ~ of biological importance (LA) 507
Fluorene, Unusually high barriers to rotation involving the tetrahedral carbon atom (FP) 87 [G.E. 67]
Fluorides, Solid state chemistry of ionic ~ (FP) 475 [G.E. 524]
Fluorine compounds, Pentafluoroorthosulfuric acid, $HOSF_5$ (SC) 44 [G.E. 56]
Fluorosulfinylimidosulfur oxide difluoride (SC) 311 [G.E. 338]
Fluoro-organic compounds, Synthesis of ~ by high-temperature conversion of saturated, unsaturated, aromatic, and heterocyclic fluorine compounds (LA) 634
Fluorosulfinyl isocyanate (SC) 110 [G.E. 88]
D-Forosamine, Synthesis of ~, the 4-dimethylamino sugar from spiramycin (SC) 302 [G.E. 301]
Food Science, Principles of ~, Part 1: Food chemistry (Book Review) 709
Four-component condensation, Synthesis of an isomer-free tetravaline derivative by stereoselective ~ and exponential multiplication of selectivity (SC) 627 [G.E. 644]
Fourier spectroscopy, Far-infrared ~ as a method for structure determination in chemistry (FP) 25 [G.E. 1]
Furan derivatives, Synthesis of ~ from 4-Benzoyloxy-1,3-dioxolane derivatives (SC) 682 [G.E. 718]

GADOLINIUM chloride, Monochlorides of the lanthanoids: ~ and TbCl (SC) 624 [G.E. 685]
D-Galactosamine, Synthesis of α-glycosidically linked disaccharides of ~ (SC) 440 [G.E. 478]
Games, Das Spiel—Naturgesetze steuern den Zufall (Book Review) 448
Gas chromatography, Sequence analysis of polypeptides and proteins by combined ~-mass spectrometry (FP) 75 [G.E. 74]
Gas/metal interfaces, Elementary processes at ~ (FP) 391 [G.E. 423]
Gauche-block structures, Kink-block structures and ~ of bimolecular films (FP) 575 [G.E. 628]
General chemistry, Allgemeine und anorganische Chemie (Book Review) 319
Genetics and biological evolution (LA) 707
Germanium compounds, $Ge_4S_6Br_4$—The first sulfide halide of germanium (SC) 162 [G.E. 162]
Triorganophosphane-dichloro- and -dibromogermanediyl and -stannanediyl: phosphane-stabilized Ge^{II} and Sn^{II} halides (SC) 308 [G.E. 303]
Novel redox reactions of tri-tert-butyl phosphane with tetrahalides of germanium and tin (SC) 308 [G.E. 304]
Germaphospholanes, Inversion at phosphorus in sila-, germa- and stannaphospholanes (SC) 429 [G.E. 445]
Germyl compounds, Electron impact induced ether cleavage by anchimeric participation of silyl and germyl groups (SC) 705 [G.E. 726]
Germyldiimine, Bis(trimethylgermyl)diimine (SC) 236 [G.E. 257]
Germylene complexes, Carbene-analogous ~ (SC) 684 [G.E. 720]
Glass—a continuing challenge to chemistry (FP) 346 [G.E. 365]
Glutamic acid, The interrelationship between arginine, ~, and proline in metabolism and nutrition (LA) 707
Gold chemistry, Is ~ a topical field of study? (FP) 728 [G.E. 830]

HALIDE complexes, Gaseous chloride complexes with halogen bridges—homo-complexes and hetero-complexes (FP) 713 [G.E. 775]
β-Halogenated alkyl esters, A new technique of protecting groups—cleavage of ~ with supernucleophilic cobalt(I)-phthalocyanine (SC) 681 [G.E. 717]
Halobacteria, Biosynthesis of the purple membrane of ~ (FP) 187 [G.E. 203]
Handbook of chemistry and physics (Book Review) 178
Handbook of organic reagents in inorganic analysis (Book Review) 786
Hemoglobin, Molecular aspects of sickle cell disease (FP) 749 [G.E. 821]
Heptalene, Cycloadditions of pentalene and azulene—A facile ~ synthesis (SC) 104 [G.E. 121]
Crystal and molecular structure of dimethyl 1,2-~ dicarboxylate (SC) 106 [G.E. 123]
Hetero Cope rearrangements, with dipolar intermediates (SC) 301 [G.E. 300]
Allylation of 4-hydroxyarsenin—arsenic-carbon ~ (SC) 690 [G.E. 728]
Heterocycles, Cumulated ylides as building blocks for the synthesis of ~ (SC) 115 [G.E. 92]
Conformational studies on twelve-membered ~. Crystal structure of 5,18-dimethyl-5,18-diazatribenzo[a,e,i]cyclododecene-6,17(5H,18H)-dione (SC) 757 [G.E. 798]
Heterocyclotetraaromatics, CuF_2-assisted synthesis of ~ by nucleophilic aromatic substitution (SC) 500 [G.E. 513]
Hexafluorophosphate, Solvolysis of the ~ ion and the structure of [tris(μ-difluorophosphato)bis(pentamethylcyclopentadienylrhodium)] ~ (SC) 490 [G.E. 506]
Hexafluororhenium(VII), $[ReF_6]^+$ (SC) 159 [G.E. 190]
1,2,3,5-Hexatetraene, Synthesis (SC) 628 [G.E. 687]
Hormone receptors (FP) 741 [G.E. 790]
Hormones, Survey of hormone-receptor interactions (LA) 318
Hydrazines, Radical cations of tetrasilyl-substituted ~ (SC) 700 [G.E. 766]
Hydrazones, Asymmetric synthesis of α-substituted ketones by metalation and alkylation of chiral ~ (SC) 549 [G.E. 579]
Hydrides, Selective reductions with complex ~ (LA) 389
Hydrocarbon cation, The cyclohept[a]acenaphthylenylium ion (SC) 240 [G.E. 262]
Hydrogenation, Selective ~ of 1,1-disubstituted cyclopropanes (SC) 373 [G.E. 415]
Hydrogen bond, The $H_5O_2^+$ ion in hydrogen bromide dihydrate (SC) 491 [G.E. 507]
Hydrogen chloride, Use of crosslinked poly(4-vinylpyridine) as ~ acceptor (SC) 163 [G.E. 192]
Hydrogen peroxide, Continuous electrocatalytic synthesis of phenol from benzene and ~ (SC) 294 [G.E. 306]
Hydrogen sulfide, Pentacarbonylmonosulfanetungsten, $W(CO)_5SH_2$ (SC) 366 [G.E. 375]
Reaction between molybdate(VI), cyanide, and ~ (SC) 784 [G.E. 855]
Hydrophobic interactions between metal complexes of aromatic ligands and 3-(trimethylsilyl)-1-propanesulfonate and their ^{1}H-NMR spectroscopic detection (SC) 548 [G.E. 585]
Hydroxymethylation, Doubly metalated methanol—A nucleophilic ~ reagent (SC) 438 [G.E. 484]
Hydrozirconation: A new transition metal reagent for organic synthesis (FP) 333 [G.E. 402]
Hyperconjugation, A new probe for C—C ~: ^{13}C-NMR on paramagnetic metallocenes (SC) 554 [G.E. 575]

IMIDAZOLE, Reaction of magnesium porphyrinates in polymers containing ~ (SC) 551 [G.E. 616]
Imines, Reactions of azines and ~ with dienophiles (LA) 564
Industrial chemistry, Technische Chemie—Eine Einführung in die chemische Reaktionstechnik (Book Review) 246
Industrial organic chemistry, Industrielle Organische Chemie (Book Review) 709
Inorganic analysis, Handbook of organic reagents in ~ (Book Review) 786
Inorganic chemistry, Allgemeine und anorganische Chemie (Book Review) 319
Insulin (LA) 57
Intercalation compounds of zirconium phosphate (SC) 544 [G.E. 608]
Intermediates, Use of the isoselectivity principle for distinguishing cationic- and σ complexes (SC) 237 [G.E. 258]
Inversion at phosphorus in sila-, germa- and stannaphospholanes (SC) 429 [G.E. 445]
Inversion barriers, Conformations and N-~ in tropane compounds (SC) 545 [G.E. 574]
Iodine azide, Isolation and infrared spectrum (SC) 553 [G.E. 612]
Iodine tris(trifluoroacetate), Selective oxidation of alkanes and ethers with ~ (SC) 436 [G.E. 478]
Ion exchange chromatography, Chlorine isotope effects in ~ (SC) 55 [G.E. 54]
Ionization, Li^+-attachment—a soft ~ method in field desorption mass spectrometry (SC) 696 [G.E. 762]
Ion structure, Collisional activation mass spectrometry—a new probe for determining ~ in the gas phase (FP) 509 [G.E. 589]
Iridium complexes, $[Ir\{2,4,6\text{-}C_6H_2(CH_3)_3\}(CO)(PPh_3)_2]$—The first example of cis-trans isomerism in complexes of the Vaska type (SC) 110 [G.E. 127]
Iridium compounds, Cyclohexenyl(1,5-cyclooctadiene)iridium—η-diene hydride or enyl structure (SC) 702 [G.E. 768]
Iron complexes, $C_{12}H_{10}O$ and thermolabile $C_{11}H_{10}O$ ketones from bullvalene via carbonyl-~ (SC) 376 [G.E. 375]
A CH carbene-~ by metal-induced fragmentation of two bonds of a bicyclopentane unit (SC) 609 [G.E. 640]
Oxidative addition of the central bond of a bicyclopentane system to iron (SC) 610 [G.E. 641]
Tris[dicarbonyl(η-cyclopentadienyl)ferrio]-stibane—A 5B-element base with total transition-metal substitution (SC) 618 [G.E. 680]
trans-Bromo(tetracarbonyl)ferrocenylcarbynetungsten (SC) 683 [G.E. 719]
μ-Thiadiborolenebis(η-cyclopentadienyliron)—preparation and structure of a new triple-decker sandwich complex (SC) 779 [G.E. 850]
Iron compounds, Structure and absolute configuration of an organo-iron compound having iron as chiral center (SC) 776 [G.E. 847]
Disodium tetracarbonylferrate (LA) 177
IR Spectroscopy, Raman IR Atlas organischer Verbindungen (Book Review) 508
IR-Spektroskopie—Eine Einführung (Book Review) 566
Isocyanides, Oxidation of 5-aminotetraazoles, a new route to ~ (SC) 113 [G.E. 89]
Isodiazene, Existence of isomeric diazenes (diimines) (SC) 385 [G.E. 386]
Structure of an "isodiimine" complex: bis-

(trimethylsilyl)-~-bis(cyclopentadienyl)-vanadium (SC) 387 [G.E. 384]
Isoselectivity principle. Use for distinguishing cationic π- and σ complexes (SC) 237 [G.E. 258]
Isothiocyanates. Three-component reactions with aryl ~. Synthesis of 5-arylimino-1,2,4-thiadiazolidin-3-ones (SC) 489 [G.E. 510]
Isotope effects. Chlorine ~ in ion exchange chromatography (SC) 55 [G.E. 54]
Isotopic substitution. Influence on diffusion in liquids (LA) 634
2-Isoxazolines. Eliminative ring opening of ~: a new route to α,β-unsaturated ketones (SC) 50 [G.E. 27]

KETENE. Rate of acid formation from phenyl-~-s in aqueous solution (SC) 380 [G.E. 413]
Competing cycloadditions in the reaction of acetylazobenzene with diphenyl-~ (SC) 432 [G.E. 449]
Molecular structure of $C_5H_5Mn(CO)_2[(C_6H_5)_2C=C=O]$. Out-of-plane deformation of the diphenyl-~ ligand (SC) 615 [G.E. 652]
Carbonyl-η-cyclopentadienyl-(4-methylphenylketenyl)bis(trimethylphosphane)-tungsten—A novel, stable transition metal-substituted ~ (SC) 632 [G.E. 649]
Ketones. Catalyzed addition of aldehydes to activated double bonds—a new synthetic approach (FP) 639 [G.E. 695]
Eliminative ring opening of 2-isoxazolines: a new route to α,β-unsaturated ~ (SC) 50 [G.E. 27]
$C_{12}H_{10}O$ and thermolabile $C_{11}H_{10}O$ ~ from bullvalene via carbonyliron complexes (SC) 376 [G.E. 375]
Enols from Norrish type II cleavage of carbonyl compounds in solution (SC) 435 [G.E. 445]
Asymmetric synthesis of α-substituted ~ by metalation and alkylation of chiral hydrazones (SC) 549 [G.E. 579]
The stereospecific formation of cyclic ~ (LA) 707
Kinetics. Rate of acid formation from phenylketenes in aqueous solution (SC) 380 [G.E. 413]
Auswertung und Analyse kinetischer Messungen (Book Review) 247
Kink-block and gauche-block structures of bimolecular films (FP) 575 [G.E. 628]

LABORATORY practice. Laborpraxis—Quantitative Analyse (Book Review) 787
β-Lactams. Synthesis (LA) 564
Lactose synthase. Protein-protein interactions in the regulation of ~ (LA) 707
Layer compounds. Kink-block and gauche-block structures of bimolecular films (FP) 575 [G.E. 628]
Electronic properties of some chain and ~ (LA) 446
Leaving groups. Nitrogen as ~: aliphatic diazonium ions (FP) 251 [G.E. 273]
Legumin. The legume storage proteins ~ and vicilin (LA) 318
Life. Search for ~ in the solar system (LA) 245
Ligand properties. The ambident ~ of bis(trimethylphosphoranylidene)methane (SC) 502 [G.E. 542]
Linear "free energy" relationships. Differences in the temperature dependence of reaction parameters in ~ (SC) 688 [G.E. 723]
N-Lithioaminofluorosilane. Synthesis (SC) 313 [G.E. 304]
Lithium complexes. A lithium-cobalt bimetal complex (SC) 46 [G.E. 50]
Lithium compounds. α-Hydroxycarboxamides from N,N-bis(methoxymethyl)carbamoyllithium and carbonyl compounds (SC) 293 [G.E. 296]
Nucleophilic aminoalkylation. Lithiated N,N-dimethylthiopivalamide (SC) 313 [G.E. 339]
Doubly metalated methanol—A nucleophilic hydroxymethylation reagent (SC) 438 [G.E. 484]
C—C linkage of polyfunctional molecules by nucleophilic addition of dianions. Synthesis of pillarose (SC) 439 [G.E. 477]
Reaction of N-protected succinimides with α-lithiated acetic acid derivatives (SC) 626 [G.E. 642]
Li^+-attachment—a soft ionization method in field desorption mass spectrometry (SC) 696 [G.E. 762]
Bis(η-1,5-cyclooctadiene)cobaltlithium (SC) 767 [G.E. 808]
Additions of lithium organocuprates as models for electron-transfer processes (LA) 446

MACROCYCLIC ligands. Transition metal complexes of synthetic ~ (LA) 120
Macromolecules. Penetration and crosslinking of ~ (FP) 451 [G.E. 487]
Magnesium complexes. A novel hetero-bimetallic dinitrogen complex (SC) 612 [G.E. 648]
Magnesium compounds. The magnesium derivative of thioacrolein dianion. A facile entry to vinyl- and divinyloxiranes (SC) 437 [G.E. 449]
Malondialdehyde. Synthesis of alkylidene-~ tetramethyl bisacetals (SC) 113 [G.E. 88]
Manganese complexes. Tetracarbonylcobaltiopentacarbonylmanganiomercury, $(CO)_4Co—Hg—Mn(CO)_5$ (SC) 162 [G.E. 188]
$Mn_2(CO)_{10}CH_2N_2$, a stable organometallic derivative of diazomethane (SC) 164 [G.E. 191]
μ-Methanediazo-(N,N,N')-tris(tetracarbonylmanganese) (SC) 368 [G.E. 379]
Thiadiborolenebis(tricarbonylmanganese)—A cluster with triple-decker structure (SC) 434 [G.E. 451]
Dimethylcarbene- and methylphenylcarbene-dicarbonyl(η-cyclopentadienyl)manganese (SC) 543 [G.E. 584]
Molecular structure of $C_5H_5Mn(CO)_2[(C_6H_5)_2C=C=O]$. Out-of-plane deformation of diphenylketene ligand (SC) 615 [G.E. 652]
Simple synthesis of dicarbonyl(η-cyclopentadienyl)-(3,3-di-tert-butylallenylidene)-manganese (SC) 624 [G.E. 684]
Manganese dioxide. Oxidation of organic compounds with active ~ (LA) 446
Mannich reaction. New variant (SC) 239 [G.E. 261]
Mass spectrometry. Sequence analysis of polypeptides and proteins by combined gas chromatography-~ (FP) 75 [G.E. 74]
Collisional activation ~—a new probe for determining the structure of ions in the gas phase (FP) 509 [G.E. 589]
Li^+-attachment—a soft ionization method in field desorption ~ (SC) 696 [G.E. 762]
Electron impact induced ether cleavage by anchimeric participation of silyl and germyl groups (SC) 705 [G.E. 726]
Progress in ~ (Book Review) 58, 566
Mathematics. Mathematik für Naturwissenschaftler (Book Review) 449
Membrane proteins. Role in anion transport in erythrocytes (LA) 446
Membranes. Techniques of chemistry. Vol. VII: ~ in separations (Book Review) 247
Mercury compounds. Tetracarbonylcobaltiopentacarbonylmanganiomercury, $(CO)_4Co—Hg—Mn(CO)_5$ (SC) 162 [G.E.
Metallocenes. New probe for C—C hyperconjugation: ^{13}C-NMR on paramagnetic ~ (SC) 554 [G.E. 575]
Metavanadate ion. Structure of the "true" ~ (SC) 374 [G.E. 385]
1,6-Methano[10]annulene. 1H-Cyclopropa[a]-naphthalene from 2,3-benzo-~ (SC) 613 [G.E. 643]
Methanol. Doubly metalated ~—A nucleophilic hydroxymethylation reagent (SC) 438 [G.E. 484]
Methionine-enkephalin. Total synthesis (SC) 297 [G.E. 332]
Methodicum Chimicum (Book Review) 120
Methylenation of [2.2]paracyclophane-1,9-diene and [2.2]paracyclophane (SC) 166 [G.E. 153]
Methylmalonyl-CoA mutase. Synthesis, structure determination, and rearrangement of a model for the active site of ~ with incorporated substrate (SC) 561 [G.E. 613]
Microbial transformations of nonsteroid cyclic compounds (Book Review) 786
Microbiological synthesis of (+)-cis-1,2-dihydroxy-1,2-dihydronaphthalene-2-carboxylic acid (SC) 549 [G.E. 581]
$β_2$-Microglobulin. Structure and significance (LA) 506
Isolation, properties, and distribution (LA) 507
Mink, Mustelan, the malodorous substance from the anal gland of the ~ (Mustela vison) and the polecat (Mustela putorius) (SC) 242 [G.E. 228]
Mitochondria. Bioenergetics of ~ in brown adipose tissue (LA) 318
Molecular geometry. Molekülgeometrie (Book Review) 318
Molecular orbital calculations. Predictive ~ in organic chemistry (FP) 519 [G.E. 602]
Molecular spectroscopy. The theory of ~ (Book Review) 635
Molybdenum. Reaction mechanism of enzymes containing ~ (LA) 388
Molybdenum complexes. trans-Pentacarbonylrhenio(phenylcarbyne)tetracarbonylmolybdenum: a transition metal carbyne complex containing a metal-metal bond (SC) 157 [G.E. 163]
1-Naphthyl rotation and metal-centered rearrangement in square-pyramidal ~ (SC) 316 [G.E. 342]
Complete asymmetric synthesis and absolute configuration of an aminoacylmolybdenum complex (SC) 495 [G.E. 511]
π-Complexes of λ^5-phosphorins with tricarbonylchromium, tricarbonylmolybdenum, or tricarbonyltungsten (SC) 503 [G.E. 543]
The photochemical addition of acetylene to tricarbonyl(η^5-cyclopentadienyl)methylmolybdenum and -tungsten (SC) 759 [G.E. 800]
Reaction between molybdate(VI), cyanide, and hydrogen sulfide (SC) 784 [G.E. 855]
Molybdenum compounds. Anion structure of tetrabutylammonium octamolybdate $[N(C_4H_9)_4]_4Mo_8O_{26}$ (SC) 375 [G.E. 385]
Functional transition-metal phosphanes (SC) 769 [G.E. 809]
Multilayers. Polymerization of tricosa-10,12-diynoic acid in ~ (SC) 764 [G.E. 805]
Mustelan, the malodorous substance from the anal gland of the mink (Mustela vison) and the polecat (Mustela putorius) (SC) 242 [G.E. 228]

NAPHTHALENE-2-carboxylic acid. Microbiological synthesis of (+)-cis-1,2-dihydroxy-1,2-dihydro-~ (SC) 549 [G.E. 581]
Naphthalene 1,2;3,4-dioxide, syn- and anti-~ (SC) 229 [G.E. 268]
Naphthalene 1,4-endoperoxide (SC) 228 [G.E. 262]
[2.2](1,4)Naphthalenophane. Intramolecular [4+4]photocycloaddition (SC) 441 [G.E. 482]
5H-Naphtho[1,8-bc]thiophen-5-one. Heterocyclic systems with 12π-electrons (SC) 775 [G.E. 810]
1-Naphthylamine. Photochemical liberation from cis-dichlorobis(1-naphthylamino)platinum(II) (SC) 625 [G.E. 686]
1-Naphthyl rotation and metal-centered rearrangement in square-pyramidal molybdenum complexes (SC) 316 [G.E. 342]
Nickel complexes. Ethylenebis(phenylsodium)nickel (SC) 47 [G.E. 51]
Structure of a bimetal-ethylene complex: $[(C_6H_5)_2NiC_2H_4]_2Na_4(THF)_5$ (SC) 48 [G.E. 52]
Bis[cyclotri(λ^5-phosphazene)dienethionato]-Ni^{II}, -Pd^{II} and -Pt^{II} complexes and their structure (SC) 488 [G.E. 505]
Carbanion complexes of nickel (SC) 621 [G.E. 682]
The anion PR_2 as single bridge between two

nickel(0) coordination centers (SC) 622 [G.E. 682]
Bis(diorganylphosphinodithioformato S,P)-nickel(II) complexes—Novel fourmembered ring chelates (SC) 768 [G.E. 811]
Nitration, Ipso attack in aromatic ~ (LA) 785
Nitriles, The analogy between O and $C(CN)_2$ (FP) 261 [G.E. 311]
Catalyzed addition of aldehydes to activated double bonds—new synthetic approach (FP) 639 [G.E. 695]
Nitrites, Na_3NO_3—Not an ortho-~ (SC) 376 [G.E. 410]
Nitroalkanes, α,α-Doubly deprotonated ~. Enhancement of the C-nucleophilicity of nitronates (SC) 505 [G.E. 540]
Nitro compounds, 1,3,2-Dioxazolidines by thermal 1,3-cycloaddition of nitro groups to strained olefins (SC) 372 [G.E. 416]
Nitrogen assimilation, Pathway of ~ in plants (LA) 564
Nitrogen complex, Novel hetero-bimetallic dinitrogen complex (SC) 612 [G.E. 648]
Nitrogen compounds, Crystal structure of a platinum complex containing NCl_2 ligands: $[Pt(NH_3)_3(NCl_2)_2Cl]Cl$ (SC) 225 [G.E. 225]
Synthesis of the $S_3N_2^+$ radical cation (SC) 226 [G.E. 226]
Fluorosulfinylimidosulfur oxide difluoride (SC) 311 [G.E. 338]
Crystal and molecular structure of the tetrasulfur pentanitride anion (SC) 379 [G.E. 411]
New cyclic SN compound: 1,1,3,3-tetraoxo-2,4-difluorosulfonylcyclodiaza-λ^6-thiane (SC) 614 [G.E. 646]
Cyclizations at electropositive silicon (SC) 619 [G.E. 647]
$[(CH_3)_3SiNH]_2PN_3S_2$: An unusual dark blue sulfur nitrogen phosphorus compound (SC) 696 [G.E. 763]
S_4N_4 bridge ligand: structure of $CuCl \cdot S_4N_4$ (SC) 765 [G.E. 807]
Synthesis and structure of a hexaazadiphosphadiarsatricyclodecane (SC) 701 [G.E. 768]
Nitrogen-phosphorus ylide, Structure of a ~ having twofold coordinated phosphorus (SC) 687 [G.E. 723]
Nitrogen transfer from a diazoalkane to a metal center (SC) 695 [G.E. 761]
Nitroso compounds, X-ray structure analysis of r-9,7,2-chloro-c-2-nitroso-trans-decalin-9-carbonitrile (SC) 760 [G.E. 802]
Partial asymmetric diels-Alder reaction with an α-chloronitroso compound (SC) 760 [G.E. 801]
Nitrosyl chloride, Reactions with arenetricarbonylchromium complexes (SC) 617 [G.E. 651]
NMR spectroscopy, Magnetic nonequivalence of the C atoms of prochiral diphenylmethyl groups in ^{13}C-~ (SC) 234 [G.E. 256]
Correlation between the β-effect of methyl groups on $\delta(^{13}C)$ and the C_α—C_β π-bond order (SC) 303 [G.E. 335]
Hydrophobic interactions between metal complexes of aromatic ligands and 3-(trimethylsilyl)-1-propanesulfonate and their ^1H-NMR spectroscopic detection (SC) 548 [G.E. 585]
New probe for C—C hyperconjugation: ^{13}C-~ on paramagnetic metallocenes (SC) 554 [G.E. 575]
Determination of the absolute configuration of chiral thiols by ^1H-~ of diastereomeric thiol esters (SC) 703 [G.E. 770]
NMR spectroscopic detection of cis and trans peptide bonds in unprotected oligo-L-proline (SC) 770 [G.E. 844]
^{13}C-~ and the determination of the conformations of biological molecules (LA) 176
~ and the periodic system (LA) 389
Dynamic ~ (Book Review) 447
2-Norbornyl cation, The σ-bridged ~ (LA) 446
Nucleophilicity, α,α-Doubly deprotonated nitroalkanes. Enhancement of the C-~ of nitronates (SC) 505 [G.E. 540]
Nucleosides, Facile preparation of 5′-cyano- and 5′-carboxy-~ (SC) 499 [G.E. 512]
C-substitution of ~ with the aid of the Eschenmoser sulfide contraction (SC) 689 [G.E. 724]
Nucleotides, Oligonucleotide synthesis on a polymeric support with avoidance of failure sequences (SC) 547 [G.E. 577]
Nutrition, Nutritional and metabolic interrelationships among sulfur compounds in avian ~ (LA) 707

OCTAHYDROINDIGO (SC) 52 [G.E. 53]
Octamolybdate, Anion structure of tetrabutylammonium ~ $[N(C_4H_9)_4]_4Mo_8O_{26}$ (SC) 375 [G.E. 385]
γ-Octose, Synthesis of the ~ of the quinocycline complex (SC) 438 [G.E. 476]
Oil, Production by hydrogenation of coal (FP) 341 [G.E. 348]
Olefin metathesis, Mechanistic Aspects (FP) 401 [G.E. 433]
CH carbene complex of iron by metal-induced fragmentation of two bonds of a bicyclopentane unit (SC) 609 [G.E. 640]
Olefins, Synthesis from α-silyl carbanions and carbonyl compounds (SC) 161 [G.E. 184]
Synthesis of phenolaldehydes with electron-rich ~ (SC) 169 [G.E. 151]
Stereospecific synthesis of β-bromoamines by ionic addition of diethyl dibromophosphoramidate to a double bond (SC) 302 [G.E. 302]
1,3,2-Dioxazolidines by thermal 1,3-cycloaddition of nitro groups to strained ~ (SC) 372 [G.E. 416]
Oligonucleotide synthesis on a polymeric support with avoidance of failure sequences (SC) 547 [G.E. 577]
Oligo-L-prolines, NMR spectroscopic detection of cis and trans peptide bonds in unprotected ~ (SC) 770 [G.E. 844]
Oligopyridines, Specific synthesis of substituted pyridines and ~ (LA) 245
Optical induction during biomimetic formation of cysteine (SC) 42 [G.E. 54]
Orbital correspondence analysis in maximum symmetry (OCAMS) (FP) 593 [G.E. 664]
Orbitals, Interaction of the Walsh ~ in bicyclopropyl (SC) 310 [G.E. 343]
Organometallic chemistry, Several annual surveys (LA) 246
Orthonitrite, Na_3NO_3—Not an ~ (SC) 376 [G.E. 410]
Oscillations, Chemical waves in the 2,4-pentanedione potassium bromate system (SC) 689 [G.E. 728]
2-Oxazolines, Synthetic utility (FP) 270 [G.E. 321]
Oxidation, Selective ~ of alkanes and ethers with iodine tris(trifluoroacetate) (SC) 436 [G.E. 478]
Radical ~ of amino acid derivatives (SC) 497 [G.E. 538]
~ of organic compounds with active MnO_2 (LA) 446
Oxidation-reduction condensations (FP) 94 [G.E. 111]
Oxidative amination of toluhydroquinone (SC) 109 [G.E. 87]
Oxygen adducts, Molecular complexes and ~ of tetrapyrrole pigments (FP) 648 [G.E. 704]
Oxygen 1,1-Bis(diphenylphosphoryl)-2,2,2-trifluoroethanol—A new intermediate of trifluoroacetyldiphenylphosphane oxidation by molecular ~ (SC) 41 [G.E. 25]
Oxygenation, Photo-~ of selenides—a new pathway to selenoxides (SC) 381 [G.E. 413]
Oxygen carriers, Synthetic ~ of biological interest (LA) 245
Oxygen complexes, Dioxygen-metal complexes (LA) 707
Oxygen compounds, Analogy between O and $C(CN)_2$ (FP) 261 [G.E. 311]
Ozone, Oxidation of alkylidenetriphenylphosphoranes with phosphite-~ adducts (SC) 298 [G.E. 297]
Oxidation of cyclopropyl hydrocarbons with ~ (SC) 761 [G.E. 802]
Effects of supersonic transport on the Earth's ~ mantle (LA) 176
Ozonides, Ozonolysis of 2,3,3a,5,6,8-hexachloro-3a,6,7,7a-tetrahydro-1,6-methano-1H-indene: isolation of a stable ~ having a 3,5-dichloro-1,2,4-trioxolane structure (SC) 433 [G.E. 479]

PALLADIUM, Cleavage of allyl ethers with Pd/C (SC) 558 [G.E. 578]
Palladium complexes, Bis[cyclotri(λ^5-phosphazene)dienethionato]-Ni^{II}, -Pd^{II} and -Pt^{II} complexes and their structure (SC) 488 [G.E. 505]
Palladium compounds, Palladium(II)-induced oligomerization of acetylenes (LA) 507
Papaverine crown ethers (SC) 685 [G.E. 722]
[2.2]Paracyclophane, Cyclopropanation of ~-s (SC) 165 [G.E. 152]
Methylenation of ~-1,9-diene and ~ (SC) 166 [G.E. 153]
Indirect determination of the half-wave reduction potentials of benzene and ~ (SC) 552 [G.E. 617]
[2.2]Paracyclophane-1,9-diene, Methylenation of ~ and [2.2]paracyclophane (SC) 166 [G.E. 153]
Pattern recognition, Chemical applications (Book Review) 178
Penetration and crosslinking of macromolecules (FP) 451 [G.E. 487]
Pentafluoroorthosulfuric acid, $HOSF_5$ (SC) 44 [G.E. 56]
Pentafulvene, [6 + 2]cycloadditions of ~. Facile pentalene synthesis (SC) 314 [G.E. 341]
Pentalene, Cycloadditions of ~ and azulene—Facile heptalene synthesis (SC) 104 [G.E. 121]
[6 + 2]cycloadditions of pentafulvene. Facile ~ synthesis (SC) 314 [G.E. 341]
2,4-Pentanedione, Chemical waves in the 2,4-~/potassium bromate system (SC) 689 [G.E. 728]
Peptides, Macrocyclic ~ in anionic polymers of amino acid N-carboxylic anhydrides (SC) 307 [G.E. 338]
NMR spectroscopic detection of cis and trans peptide bonds in unprotected oligo-L-proline (SC) 770 [G.E. 844]
Use of cyclic ~ for conformational studies (LA) 507
Peptide synthesis, Synthesis of (poly-)peptides with phosphorous diester triazolides (SC) 305 [G.E. 337]
4,6-Diphenylthieno[3,4-d][1,3]dioxol-2-one 5,5-dioxide, a novel activating agent for ~ (SC) 444 [G.E. 480]
Recovery of chiral α-ferrocenylalkylamines on stereoselective ~ by four-component condensation (SC) 492 [G.E. 509]
Synthesis of an isomer-free tetravaline derivative by stereoselective four-component condensation and exponential multiplication of selectivity (SC) 627 [G.E. 644]
Periodic system, Lehrprogramm Atombau und Periodensystem (Book Review) 709
Pharmacology, Allgemeine und spezielle Pharmakologie und Toxikologie (Book Review) 121
Phenol, Continuous electrocatalytic synthesis of ~ from benzene and hydrogen peroxide (SC) 294 [G.E. 306]
Phenolaldehydes, Synthesis of ~ with electron-rich olefins (SC) 169 [G.E. 151]
Phenols, Synthesis of 3-aryl-2,5-di-tert-butyl-2,4-cyclopentadienones by base-catalyzed oxygenation of 4-aryl-2,6-di-tert-butyl-~ (SC) 160 [G.E. 154]
Nonpollutative chlorination and chlorinating oxidation of ~ (SC) 608 [G.E. 641]
Phenylketenes, Rate of acid formation from ~ in aqueous solution (SC) 380 [G.E. 413]
Phosphanes, Triorganophosphanedichloro- and -dibromogermanediyl and -stannanediyl: phosphane-stabilized Ge^{II} and Sn^{II} halides (SC) 308 [G.E. 303]
Novel redox reactions of tri-tert-butylphosphane with tetrahalides of germanium and tin (SC) 308 [G.E. 304]
A phosphorus(III) derivative with sterically fixed bis(trimethylsilyl)amino groups (SC) 309 [G.E. 305]
Mononuclear paramagnetic biphosphinotri-

carbonylcobalt(0) complex (SC) 381 [G.E. 415]
Functional transition-metal ~ (SC) 769 [G.E. 809]
Phosphanylium chloride, First example of a chlorophosphane-~ transformation. 2-Methyl-1,2,3λ^2-diazaphosphole hydrochlorides (SC) 111 [G.E. 91]
Phosphate bonds, Coupling of "high-energy" ~ to energy transductions (LA) 58
6λ^5-Phosphatricyclo[3.3.1.0^{2,7}]non-3-ene, X-ray structure analysis of 6-methyl-6-oxo-3,5,7-triphenyl-~, the product of unusual intramolecular reactions (SC) 238 [G.E. 229]
Phosphazene, Cyclo-~ spanned by a sulfur diimido group (SC) 39 [G.E. 24]
Methylenedi-λ^5-~ by amide cleavage of tetramethylphosphonium salts (SC) 501 [G.E. 541]
The structure of a cyclotetra-~ spanned by a sulfur diimido group (SC) 783 [G.E. 853]
Phosphide complexes, The anion PR_2 as single bridge between two nickel(0) coordination centers (SC) 622 [G.E. 682]
Phosphinidene complexes as ligands (SC) 682 [G.E. 719]
Phosphite-ozone adducts, Oxidation of alkylidenetriphenylphosphoranes with ~ (SC) 298 [G.E. 297]
Phospholanes, Inversion at phosphorus in sila-, germa- and stanna-~ (SC) 429 [G.E. 445]
Phosphonium salts, A methylenedi-λ^5-phosphazene by amide cleavage of tetramethyl-~ (SC) 501 [G.E. 541]
Phosphoramidate, Stereospecific synthesis of β-bromoamines by ionic addition of diethyl dibromo-~ to a double bond (SC) 302 [G.E. 302]
Phosphoranes, Oxidation of alkylidenetriphenyl-~ with phosphite-ozone adducts (SC) 298 [G.E. 297]
(Dichloromethylene)triphenylphosphorane (SC) 315 [G.E. 340]
A tricyclic phosphorane with axial annelation (SC) 781 [G.E. 851]
Phosphorin rearrangement, X-Ray structure analysis of 6-methyl-6-oxo-3,5,7-triphenyl-6λ^5-phosphatricyclo[3.3.1.0^{2,7}]non-3-ene, the product of unusual intramolecular reactions (SC) 238 [G.E. 229]
Phosphorins, π-Complexes of λ^5-~ with tricarbonylchromium, tricarbonylmolybdenum, or tricarbonyltungsten (SC) 503 [G.E. 543]
X-Ray structure analysis of two π-complexes of λ^5-~ with tricarbonylchromium (SC) 504 [G.E. 544]
Phosphorous diester triazolides, Synthesis of (poly-)peptides with ~ (SC) 305 [G.E. 337]
Phosphorus betaines (SC) 693 [G.E. 759]
Phosphorus-carbon compounds, Chemistry of simple ~ (FP) 468 [G.E. 517]
Phosphorus compounds, 1,1-Bis(diphenylphosphoryl)-2,2,2-trifluoroethanol—A new intermediate of trifluoroacetyldiphenylphosphane oxidation by molecular oxygen (SC) 41 [G.E. 25]
First example of a chlorophosphane-phosphanylium chloride transformation: 2-methyl-1,2,3λ^2-diazaphosphole hydrochlorides (SC) 111 [G.E. 91]
Bis[cyclotri(λ^5-phosphazene)dienethionato]-Ni^{II}, -Pd^{II} and -Pt^{II} complexes and their structure (SC) 488 [G.E. 505]
Solvolysis of the hexafluorophosphate ion and the structure of [tris(μ-difluorophosphato)bis(pentamethylcyclopentadienylrhodium)]hexafluorophosphate (SC) 490 [G.E. 506]
The ambident ligand properties of bis(trimethylphosphoranylidene)methane (SC) 502 [G.E. 542]
Isolation of a diaza-λ^3,λ^5- and a thermodynamically unstable diaza-λ^5,λ^5-diphosphetidine (SC) 555 [G.E. 582]
1,3,2λ^2,4-diazaphosphoniaaluminatacyclobutane: A cyclic zwitterion having twofold coordinated phosphorus (SC) 692 [G.E. 758]
[$(CH_3)_3SiNH]_2PN_3S_2$: An unusual dark blue sulfur nitrogen phosphorus compound (SC) 696 [G.E. 763]
Synthesis and structure of a hexaazadiphosphadiarsatricyclodecane (SC) 701 [G.E. 768]
Simplified synthesis of bis(triphenylphosphoranylidene)methane (SC) 702 [G.E. 769]
Bis(diorganylphosphinodithioformato S,P)-nickel(II) complexes—novel four-membered ring chelates (SC) 768 [G.E. 811]
Synthesis and isolation of cis- and trans-1,3,2λ^3,4λ^3-diazadiphosphetidine (SC) 772 [G.E. 845]
Phosphorus ylides, Synthesis of ~ at a cobalt-complex center (SC) 42 [G.E. 61]
Base-induced intramolecular cyclization of silicon substituted ~ (SC) 367 [G.E. 376]
Structure of a phosphorus-nitrogen ylide having twofold coordinated phosphorus (SC) 687 [G.E. 723]
Phosphorylation, ~ with 1-phosphorylpyrazoles (SC) 378 [G.E. 377]
Mitochondrial ATP-phosphate exchange and the site of uncoupling of oxidative ~ (LA) 176
1-Phosphorylpyrazoles, Phosphorylation with ~ (SC) 378 [G.E. 377]
Photochemistry, Enols from Norrish type II cleavage of carbonyl compounds in solution (SC) 435 [G.E. 445]
Photochemical liberation of 1-naphthylamine from cis-dichlorobis(1-naphthylamino)platinum(II) (SC) 625 [G.E. 686]
~ of organic sulfur compounds (LA) 177
~ of thiones and the chemistry of the S_2 state (LA) 506
Solid state ~ (Book Review) 787
Aspects of organic ~ (Book Review) 787
Photocleavage, [6+6]-~ of [2.2]cyclophanes (SC) 442 [G.E. 482]
Photocycloaddition, Intramolecular [4+4]-~ of [2.2](1,4)naphthalenophane (SC) 441 [G.E. 482]
Photoelectron spectroscopy, Photoelectron spectrum of $H_2C{=}S{=}O$ (SC) 383 [G.E. 380]
Photoelectron spectrum of $HN{=}S{=}O$ (SC) 384 [G.E. 381]
Photoisomerization and photocleavage of bicyclo[4.2.0]octa-2,4-dienes (SC) 779 [G.E. 812]
Photo-oxygenation of selenides—a new pathway to selenoxides (SC) 381 [G.E. 413]
Physical chemistry, Einführung in die Physikalische Chemie (Book Review) 708
Physiological chemistry, Physiologische Chemie (Book review) 710
Pillarose, C—C linkage of polyfunctional molecules by nucleophilic addition of dianions. Synthesis of ~ (SC) 439 [G.E. 477]
Piperidine, Conformation (LA) 245
Planning of experiments, Statistische Versuchsplanung (Book Review) 389
Plastics handbook, Kunststoff-Handbuch (Book Review) 636
Plastic Waste, Processing of ~ and scrap tires into chemical raw materials, especially by pyrolysis (FP) 660 [G.E. 737]
Platinum complexes, Crystal structure of a platinum complex containing NCl_2 ligands: [Pt$(NH_3)_3(NCl_2)_2$Cl]Cl (SC) 225 [G.E. 225]
Bis[cyclotri(λ^5-phosphazene)dienethionato]-Ni^{II}, -Pd^{II} and -Pt^{II} complexes and their structure (SC) 488 [G.E. 505]
Photochemical liberation of 1-naphthylamine from cis-dichlorobis(1-naphthylamino)platinum(II) (SC) 625 [G.E. 686]
Polar effects in organic reactions (FP) 569 [G.E. 621]
Polecat, Mustelan, the malodorous substance from the anal gland of the mink (Mustela vison) and the ~ (Mustela putorius) (SC) 242 [G.E. 228]
Polyene cyclizations, Biomimetic ~ (FP) 9 [G.E. 33]
Polyethylene, Extreme bond angle distortion in organozirconium compounds active toward ethylene (SC) 629 [G.E. 688]
Halogen-free soluble Ziegler catalysts for the polymerization of ethylene. Control of molecular weight by choice of temperature (SC) 630 [G.E. 689]
Polymerizations, Zum Ablauf ionischer Polymerisationsreaktionen (Book Review) 566
Polymers, Penetration and crosslinking of macromolecules (FP) 451 [G.E. 487]
Crosslinked ~ having activated ester groups—a versatile support material (SC) 546 [G.E. 576]
Reaction of magnesium porphyrinates in ~ containing imidazole (SC) 551 [G.E. 616]
Heterogeneous ~ (LA) 176
Polyolefins, Photodegradation and stabilization of commercial ~ (LA) 177
Polypeptides, Sequence analysis of ~ and proteins by combined gas chromatography-mass spectrometry (FP) 75 [G.E. 74]
Poly(4-vinylpyridine), Use of crosslinked ~ as HCl acceptor (SC) 163 [G.E. 192]
Porphyrinates, Reaction of magnesium ~ in polymers containing imidazole (SC) 551 [G.E. 616]
Porphyrinogen, Structure of N,N′,N″,N‴-tetramethyl-2,3,7,8,12,13,17,18-octakis(carboxymethyl)-~ dihydrate (SC) 552 [G.E. 616]
Porphyrins, Molecular complexes and oxygen adducts of tetrapyrole pigments (FP) 648 [G.E. 704]
Proline, NMR spectroscopic detection of cis and trans peptide bonds in unprotected oligo-L-~ (SC) 770 [G.E. 844]
The interrelationship between arginine, glutamic acid, and ~ in metabolism and nutrition (LA) 707
Propargylic acetates, Trialkylallenes from 1,1-disubstituted ~ (SC) 496 [G.E. 537]
Propeller molecules, Stereochemical consequences of correlated rotation in ~ (LA) 317
Prostaglandins, A synthesis of ~: strategy and reality (FP) 207 [G.E. 244]
~ (LA) 245
Protecting groups, Electro-deprotection—electrochemical removal of ~ (FP) 281 [G.E. 283]
A new technique of ~—cleavage of β-halogenated alkyl esters with supernucleophilic cobalt(I)-phthalocyanine (SC) 681 [G.E. 717]
Proteins, Sequence analysis of polypeptides and ~ by combined gas chromatography-mass spectrometry (FP) 75 [G.E. 74]
Protein-protein interactions in the regulation of lactose synthase (LA) 707
Sulfenic acid groups in ~ (LA) 785
Proton, The $H_5O_2^+$ ion in hydrogen bromide dihydrate (SC) 491 [G.E. 507]
Proton pump, Bacteriorhodopsin as an example of a light-driven ~ (FP) 17 [G.E. 16]
Pterodactylane, Four linearly annelated cyclobutane rings: the tetracyclo[4.4.0.0^{2,5}.0^{7,10}]-decane system (SC) 431 [G.E. 447]
Purple membrane, Biosynthesis of the ~ of halobacteria (FP) 187 [G.E. 203]
Pyrazoles, Phosphorylation with 1-phosphoryl-~ (SC) 378 [G.E. 377]
Pyridines, Specific synthesis of substituted ~ and oligo-~ (LA) 245
Pyridinium betaines, Synthetic applications of heteroaromatic betaines with six-membered rings (FP) 1 [G.E. 41]
Pyrolysis, Processing of plastic waste and scrap tires into chemical raw materials, especially by ~ (FP) 660 [G.E. 737]
Pyrroles, New synthetic methods for monocyclic 1H-, 2H-, and 3H-~ (LA) 563

QUANTUM mechanical principles, Einführung in die Theoretische Chemie (Book Review) 390
Quantum mechanics for organic chemists (Book Review) 507
Quinocycline, Synthesis of the γ-octose of the ~ complex (SC) 438 [G.E. 476]

RADICAL anion and radical cation of a tetrasilyl-substituted ethylene (SC) 699 [G.E. 765]
Radical cation and radical anion of a tetrasilyl-substituted ethylene (SC) 699 [G.E. 765]

Radical cations, of tetrasilyl-substituted hydrazines (SC) 700 [G.E. 766]
Radicals, Temperature dependence of the selectivity of π- and σ ~ (SC) 173 [G.E. 159]
Persistent carbon-centered ~ (LA) 317
Radioimmunoassay (FP) 525 [G.E. 565]
~ of steroid hormones (Book Review) 508
Raman spectroscopy, Raman IR Atlas organischer Verbindungen (Book Review) 508
Raw materials (LA) 246
Reaction engineering, Chemische Reaktionstechnik (Book Review) 567
Reaction parameters, Differences in the temperature dependence of ~ in linear "free energy" relationships (SC) 688 [G.E. 723]
Reaction types, Reaktionstypen in der anorganischen Chemie (Book Review) 565
Rearrangement, X-Ray structure analysis of 6-methyl-6-oxo-3,5,7-triphenyl-6λ⁵-phosphatricyclo[3.3.1.0^{2,7}]non-3-ene, the product of unusual intramolecular reactions (SC) 238 [G.E. 229]
Anionic O→C ~-s in trialkylsiloxybenzenes and trialkylsiloxypyridines (SC) 428 [G.E. 444]
Receptors, Hormone ~ (FP) 741 [G.E. 790]
Survey of hormone-receptor interactions (LA) 318
Redox reactions, Novel ~ of tri-tert-butylphosphane with tetrahalides of germanium and tin (SC) 308 [G.E. 304]
Reduction potentials, Indirect determination of the half-wave ~ of benzene and [2.2]paracyclophane (SC) 552 [G.E. 617]
Rhenium complexes, μ-Bromo-μ-phenylmethylidynebis(tetracarbonylrhenium) (SC) 231 [G.E. 228]
Rhenium compounds, trans-Pentacarbonylrhenio(phenylcarbyne)tetracarbonylmolybdenum: A transition metal carbyne complex containing a metal-metal bond (SC) 157 [G.E. 163]
Hexafluororhenium(VII), $[ReFe_6]^+$ (SC) 159 [G.E. 190]
Rhodium complexes, 2,2''-Bis(diphenylphosphino)-2',3',5',6'-tetraphenyl-p-terphenyl as an arene chelate ligand for rhodium(I) (SC) 241 [G.E. 260]
Separation of deuteriated ethylenes $C_2H_{4-n}D_n$ by complexation chromatography on a rhodium(I) complex (SC) 304 [G.E. 336]
Solvolysis of the hexafluorophosphate ion and the structure of [tris(μ-difluorophosphato)bis(pentamethylcyclopentadienylrhodium)]hexafluorophosphate (SC) 490 [G.E. 506]
Ribosome structure, Chemical methods of studying ~ (FP) 533 [G.E. 555]
Ring opening, Eliminative ~ of 2-isoxazolines: a new route to α,β-unsaturated ketones (SC) 50 [G.E. 27]
Rotamers, Unusually high barriers to rotation involving the tetrahedral carbon atom (FP) 87 [G.E. 67]
Rotanes, Coupling reactions of vinylidenedicyclopropanes doubly halogenated in allylic positions—a productive synthesis of trispiro[2.0.2.0.2.0]nonane ([3]rotane) (SC) 762 [G.E. 803]
A universal rotane synthesis—hexaspiro[2.0.2.0.2.0.2.0.2.0.2.0]octadecane (SC) 763 [G.E. 804]
Rotation, Unusually high barriers to ~ involving the tetrahedral carbon atom (FP) 87 [G.E. 67]
Stereochemical consequences of correlated ~ in propeller molecules (LA) 317
Rydberg states (LA) 246

SCRAP tires, Processing of plastic waste and ~ into chemical raw materials, especially by pyrolysis (FP) 660 [G.E. 737]
Selectivity, Temperature dependence of the ~ of π- and σ radicals (SC) 173 [G.E. 159]
The isoselective relationship: limitations and prospects of the structure-~ discussion (SC) 174 [G.E. 161]
Selectivity values, Differences in the temperature dependence of reaction parameters in linear "free energy" relationships (SC) 688 [G.E. 723]
Selenides, Photo-oxygenation of ~—a new pathway to selenoxides (SC) 381 [G.E. 413]
Selenium compounds, Bond-delocalized cyclobuteneselenones (SC) 704 [G.E. 771]
Synthesis of tetrathiafulvalenes and tetraselenafulvalenes (LA) 635
Selenoxides, Photo-oxygenation of selenides—a new pathway to ~ (SC) 381 [G.E. 413]
Self-association, The ~ of tubulin (LA) 707
Separation processes, Techniques of chemistry. Vol. VII: Membranes in separations (Book Review) 247
Sequence analysis of polypeptides and proteins by combined gas chromatography-mass spectrometry (FP) 75 [G.E. 74]
Serum albumin, Biosynthesis (LA) 176
Serum proteins, Serumproteine (Book Review) 59
Sesquiterpenes formed by Solanaceae under stress conditions (LA) 564
Sickle cell disease, Molecular aspects of ~ (FP) 749 [G.E. 821]
Silanes, Tri-tert-butyl-~: reactions and hindered Si—C rotation (SC) 43 [G.E. 26]
Synthesis of N-lithioaminofluorosilane (SC) 313 [G.E. 304]
Cleavage of esters and ethers with iodotrimethylsilane (SC) 774 [G.E. 847]
Silaphospholanes, Inversion at phosphorus in ~, and germa- and stannaphospholanes (SC) 429 [G.E. 445]
Silicon compounds, Base-induced intramolecular cyclization of silicon-substituted phosphorus ylides (SC) 367 [G.E. 376]
New electrochemical method of forming SiSi bonds (SC) 370 [G.E. 414]
Hydrophobic interactions between metal complexes of aromatic ligands and 3-(trimethylsilyl)-1-propanesulfonate and their ^{1}H-NMR spectroscopic detection (SC) 548 [G.E. 585]
Cyclization reactions at electropositive silicon (SC) 619 [G.E. 647]
Radical cation and radical anion of a tetrasilyl-substituted ethylene (SC) 699 [G.E. 765]
Radical cations of tetrasilyl-substituted hydrazines (SC) 700 [G.E. 766]
Silicon-nitrogen ylide, Nucleophilic 1,3-rearrangement at silicon—Indirect evidence for a ~ (SC) 312 [G.E. 307]
(3-Siloxy-3-buten-1-ynyl)amines (SC) 51 [G.E. 59]
Silylacetylenes, Fluoride-catalyzed addition to carbonyl compounds (SC) 498 [G.E. 539]
Silylamides, Transition-metal dialkylamides and di-~ (LA) 785
Silylcadmium compound, Bis(tri-tert-butylsilyl)cadmium: The first ~ isolated in substance (SC) 620 [G.E. 681]
α-Silyl carbanions, Synthesis of olefins from ~ and carbonyl compounds (SC) 161 [G.E. 184]
Silyl compounds, A phosphorus(III) derivative with sterically fixed bis(trimethylsilyl)amino groups (SC) 309 [G.E. 305]
Electron Impact induced ether cleavage by anchimeric participation of silyl and germyl groups (SC) 705 [G.E. 726]
Silyloxy compounds, Anionic O→C rearrangements in trialkylsiloxybenzenes and trialkylsiloxypyridines (SC) 428 [G.E. 444]
Single-crystal surfaces, Reactions on ~ (LA) 635
Sodium complexes, Ethylenebis(phenylsodium)nickel (SC) 47 [G.E. 51]
Structure of a bimetal-ethylene complex: $[(C_6H_5)_2NiC_2H_4]_2Na_4(THF)_5$ (SC) 48 [G.E. 52]
Solid phase synthesis, Crosslinked polymers having activated ester groups—a versatile support material (SC) 546 [G.E. 576]
Oligonucleotide synthesis on a polymeric support with avoidance of failure sequences (SC) 547 [G.E. 577]
Spectrophotometry, Dual-wavelength ~ (FP) 673 [G.E. 750]
Spectroscopy, Far-infrared Fourier ~ as a method for structure determination in chemistry (FP) 25 [G.E. 1]
ESCA investigations on industrial catalysts (LA) 507
Theory of molecular ~ (Book Review) 635
Spin-lattice relaxation (LA) 119
Spiramycin, Synthesis of D-forosamine, the 4-dimethylamino sugar from ~ (SC) 302 [G.E. 301]
Spiro compounds, Synthesis of carbocyclic ~ (LA) 635
Squalene, The crystal structure of ~ (SC) 778 [G.E. 851]
Stannaphospholanes, Inversion at phosphorus in sila- and germaphospholanes and ~ (SC) 429 [G.E. 445]
Stereoisomerism, Isolation of conformational diastereoisomers of N,N',N''-tribenzyltrianthranilide (SC) 223 [G.E. 223]
Steroid hormones, Radioimmunoassay of ~ (Book Review) 508
Storage proteins, The legume ~ legumin and vicilin (LA) 318
Structural determination, Correlation tables for the ~ of organic compounds (Book Review) 179
Subnuclear components (Book Review) 636
Substituent effects, Concept of allopolarization. ~ on the reactions of ambifunctional anions (FP) 321 [G.E. 389]
Polar effects in organic reactions (FP) 569 [G.E. 621]
Succinimides, Reaction of N-protected ~ with α-lithiated acetic acid derivatives (SC) 626 [G.E. 642]
Sulfenic acid groups in proteins (LA) 785
Sulfide contraction, C-substitution of nucleosides with the aid of the Eschenmoser ~ (SC) 689 [G.E. 725]
Sulfides, Isolation of crystalline bis(thioacyl)~ (SC) 766 [G.E. 844]
Sulfine, Photoelectron spectrum of $H_2C{=}S{=}O$ (SC) 383 [G.E. 380]
Sulfinyl imide, Photoelectron spectrum of $HN{=}S{=}O$ (SC) 384 [G.E. 381]
Sulfur compounds, Fluorosulfinylimidosulfur oxide difluoride (SC) 311 [G.E. 338]
Crystal and molecular structure of the tetrasulfur pentanitride anion (SC) 379 [G.E. 411]
Synthesis of thiepino[4,5-c]pyrrole derivatives having sulfur in different oxidation states (SC) 382 [G.E. 419]
A new cyclic SN compound: 1,1,3,3-tetraoxo-2,4-difluorosulfonylcyclodiaza-λ⁶-thiane (SC) 614 [G.E. 646]
$[(CH_3)_3SiNH]_2PN_3S_2$: An unusual dark blue sulfur nitrogen phosphorus compound (SC) 696 [G.E. 763]
S_4N_4 bridge ligand: structure of $CuCl{\cdot}S_4N_4$ (SC) 765 [G.E. 807]
Synthesis of cycloheptasulfur oxide, S_7O (SC) 772 [G.E. 854]
Photochemistry of organic ~ (LA) 177
Nutritional and metabolic interrelationships among ~ in avian nutrition (LA) 707
Sulfur diimide, The structure of a cyclotetraphosphazene spanned by a sulfur diimido group (SC) 783 [G.E. 853]
Sulfur-nitrogen compounds, Synthesis of the $S_3N_2^+$ radical cation (SC) 226 [G.E. 226]
Surface, Crystal face dependence of the ~ chemistry of tungsten (LA) 177
Surface reactions, Elementary processes at gas/metal interfaces (FP) 391 [G.E. 423]
Synthetic methods, Synthetic applications of heteroaromatic betaines with six-membered rings (FP) 1 [G.E. 41]
The synthetic utility of 2-oxazolines (FP) 270 [G.E. 321]
Hydrozirconation: A new transition metal reagent for organic synthesis (FP) 333 [G.E. 402]
Catalyzed addition of aldehydes to activated double bonds—a new synthetic approach (FP) 639 [G.E. 695]
Synthesis, Les grandes reactions de la synthese organique (Book Review) 179

TELLURIUM compounds, Crystal structure of $Te_5O_4F_{22}$ (SC) 771 [G.E. 846]
Tellurium(IV) iodide: Tetrameric Te_4I_{16} molecules in the solid (SC) 39 [G.E. 28]
Terbium chloride, Monochlorides of the lanthanoids: GdCl and ~ (SC) 624 [G.E. 685]
p-Terphenyl, 2,2''-Bis(diphenylphosphino)-2',3',5',6'-tetraphenyl-~ as an arene chelate ligand for rhodium(I) (SC) 241 [G.E. 260]
Tetraazacycloalkane-N,N',N'',N'''-tetraacetic acids, Complex formation with ~ as a function of ring size (SC) 686 [G.E. 760]
Tetraazoles, Oxidation of 5-amino-~, a new route to isocyanides (SC) 113 [G.E. 89]
Tetracyclo[4.4.0.0^{2,5}.0^{7,10}]decane, Four linearly annelated cyclobutane rings: the ~ system (SC) 431 [G.E. 447]
5,6,9,10-Tetrahydrobenzocyclooctene, the simplest known planar neutral conjugated eight-membered carbocycle (SC) 117 [G.E. 126]
2-(2,4,5,7-Tetranitro-9-fluorenylideneaminooxy)propionic acid, Absolute configuration (SC) 115 [G.E. 93]
Tetrapyrrole pigments, Molecular complexes and oxygen adducts of ~ (FP) 648 [G.E. 704]
Tetraselenafulvalenes, Synthesis of tetrathiafulvalenes and ~ (LA) 635
Tetrathiafulvalenes, Synthesis of ~ and tetraselenafulvalenes (LA) 635
Tetrathiotungstatostannate, Dimeric bis-~—A novel coordination compound with nonequivalent and tridentate WS_4^{2-} ligands (SC) 633 [G.E. 691]
Tetravaline derivative, Synthesis of an isomer-free ~ by stereoselective four-component condensation and exponential multiplication of selectivity (SC) 627 [G.E. 644]
2H-1-Thiacyclobutabenzene, Synthesis of the ~ system (SC) 117 [G.E. 94]
3H-1λ^4,2,6-thiadiazine, X-ray structure analysis of a 4,5-dihydro-~ (SC) 782 [G.E. 852]
1,2,4-Thiadiazolidine oxides, Novel 1,2,4-thiadiazolidine 1-oxides and 1,1-dioxides from 2-imino-1,3-thiazetidines (SC) 103 [G.E. 120]
1,2,4-Thiadiazolidin-3-ones, Three-component reactions with aryl isothiocyanates. Synthesis of 5-arylimino-~ (SC) 489 [G.E. 510]
1,2,5-Thiadiborolene, Thiadiborolenebis(tricarbonylmanganese)—A cluster with triple-decker structure (SC) 434 [G.E. 451]
μ-Thiadiborolenebis(η-cyclopentadienyliron—preparation and structure of a new triple-decker sandwich complex (SC) 779 [G.E. 850]
5-Thiariboflavins, 5-Deazariboflavins and ~: a simple pathway to antimetabolites of vitamin B_2 (SC) 443 [G.E. 475]
1,3-Thiazetidines, Novel 1,2,4-thiadiazolidine 1-oxides and 1,1-dioxides from 2-imino-~ (SC) 103 [G.E. 120]
Thiazole, New ring transformation of zwitterionic bicyclic ~ systems (SC) 494 [G.E. 511]
Thieno[3,4-d][1,3]dioxol-2-one, 4,6-Diphenyl-~ 5,5-dioxide, a novel activating agent for peptide syntheses (SC) 444 [G.E. 480]
Thiepin, Low-temperature X-ray structure analysis of 1-benzo-~ (SC) 297 [G.E. 295]
New synthetic entry to the ~ system.—Benzo[d]-~ and dibenzo[bd]-~ (SC) 611 [G.E. 650]
Thiepino[4,5-c]pyrrole, Synthesis of ~ derivatives having sulfur in different oxidation states (SC) 382 [G.E. 419]
Thietane, Mustelan, the malodorous substance from the anal gland of the mink (Mustela vison) and the polecat (Mustela putorius) (SC) 242 [G.E. 228]
Thioacrolein dianion, The magnesium derivative of ~. A facile entry to vinyl- and divinyloxiranes (SC) 437 [G.E. 449]
(Thioacyl)sulfides, Isolation of crystalline bis-~ (SC) 766 [G.E. 844]
Thioformaldehyde S-oxide, Photoelectron spectrum of $H_2C{=}S{=}O$ (SC) 383 [G.E. 380]
Thioformates, Bis(diorganylphosphinodithioformato-S,P)nickel(II) complexes—Novel four-membered ring chelates (SC) 768 [G.E. 811]
Thioketene, X-Ray structure analysis of a dialkyl-~ (SC) 40 [G.E. 25]
Thiols, Determination of the absolute configuration of chiral ~ by ^{1}H-NMR spectroscopy of diastereomeric thiol esters (SC) 703 [G.E. 770]
Thiometalate ions, Complexes having ~ as bridging ligands (SC) 680 [G.E. 725]
Thiones, Photochemistry of ~ and the chemistry of the S_2 state (LA) 506
Thionitrosyl cation, The ~ NS^+ as a synthetic reagent (SC) 691 [G.E. 757]
Thiopivalamide, Nucleophilic aminoalkylation. Lithiated N,N-Dimethyl-~ (SC) 313 [G.E. 339]
Tin compounds, Triorganophosphanedichloro- and -dibromogermanediyl and -stannanediyl: phosphane-stabilized Ge^{II} and Sn^{II} halides (SC) 308 [G.E. 303]
Novel redox reactions of tri-tert-butylphosphane with tetrahalides of germanium and tin (SC) 308 [G.E. 304]
Dimeric bistetrathiotungstatostannate—A novel coordination compound with nonequivalent and tridentate WS_4^{2-} ligands (SC) 633 [G.E. 691]
Toluhydroquinone, Oxidative amination (SC) 109 [G.E. 87]
Toxicology, Biochemical aspects of the ~ of cadmium (LA) 446
Allgemeine und spezielle Pharmakologie und Toxikologie (Book Review) 121
Trace analysis, Application of catalyzed reactions in analytical chemistry (FP) 150 [G.E. 177]
Transcarboxylase, Subunit-subunit interactions of ~ (LA) 707
trans-Decalin-9-carbonitrile, X-ray structure analysis of r-9,t-2-chloro-c-2-nitroso-~ (SC) 760 [G.E. 802]
Transition metals, The use of ~ in organic synthesis (LA) 785
Transport phenomena (Book Review) 389
Trianthranilide, Isolation of conformational diastereoisomers of N,N',N''-tribenzyl-~ (SC) 223 [G.E. 223]
Triazolides, Synthesis of (poly-)peptides with phosphorous diester ~ (SC) 305 [G.E. 337]
Triborylamine, Tris(3-methylborolan-1-yl)-amine, an electron-deficient ~ (SC) 235 [G.E. 231]
Tricosa-10,12-diynoic acid, Polymerization of ~ in multilayers (SC) 764 [G.E. 805]
Tricyclo[5.3.0.0^{2,10}]deca-3,5-diene, Degenerate butadienylcyclopropane rearrangement in ~ (SC) 53 [G.E. 63]
Tricyclo[4.1.0.0^{2,7}]heptenyl cation—a new isomer of the tropylium ion (SC) 493 [G.E. 508]
syn-Tricyclo[5.1.0.0^{2,4}]oct-5-ene-3,8-dicarboxylate (SC) 163 [G.E. 185]
Trifluoroacetylation of amines with N-trifluoroacetyl-Nylon 66 (SC) 777 [G.E. 848]
3,7,10-Trioxapentacycloundecane, 3,7,10-Trioxapentacyclo[3.3.3.0^{2,4}.0^{6,8}.0^{9,11}]-undecane (3,7,10-Trioxatrishomobarrelene) (SC) 686 [G.E. 721]
3,7,10-Trioxatrishomobarrelene,3,7,10-Trioxapentacyclo[3.3.3.0^{2,4}.0^{6,8}.0^{9,11}]-undecane (~) (SC) 686 [G.E. 721]
cis-Trioxatris-σ-homotropilidene, Synthesis (SC) 559 [G.E. 611]
1,2,4-Trioxolane, Ozonolysis of 2,3,3a,4,5,8-hexachloro-3a,6,7,7a-tetrahydro-1,6-methano-1H-indene: isolation of a stable ozonide having a 3,5-dichloro-~ structure (SC) 433 [G.E. 479]
Triple-decker complexes, Novel type of ~—borole as bridging ligand (SC) 433 [G.E. 450]
μ-Thiadiborolenebis(η-cyclopentadienyliron)—preparation and structure of a new triple-decker sandwich complex (SC) 779 [G.E. 850]
Thiadiborolenebis(tricarbonylmanganese)—A cluster with triple-decker structure (SC) 434 [G.E. 451]
Triptycene, Unusually high barriers to rotation involving the tetrahedral carbon atom (FP) 87 [G.E. 67]
Triquinacene, Stability of triquinacenyl cations and triquinacenyl radicals (SC) 556 [G.E. 609]
Bridgehead cations of tricyclo[5.2.1.0^{4,10}]-deca-2,5,8-triene (triquinacene) (SC) 557 [G.E. 610]
Triquinacenyl cations, Stability of ~ and triquinacenyl radicals (SC) 556 [G.E. 609]
Bridgehead cations of tricyclo[5.2.1.0^{4,10}]-deca-2,5,8-triene (triquinacene) (SC) 557 [G.E. 610]
Triscyclobuta[b,h,n]triphenylene, 10,11-Dihydrocyclobuta[b]triphenylene and 1,2,5,6,9,10-hexahydro-~ (SC) 53 [G.E. 63]
Trishomobarrelene, Optically active bridgehead derivatives of ~ and trishomobullvalene (SC) 429 [G.E. 446]
Trishomobullvalene, Optically active bridgehead derivatives of trishomobarrelene and ~ (SC) 429 [G.E. 446]
Tropane, Conformations and N-inversion barriers in ~ compounds (SC) 545 [G.E. 574]
Tubulin, The self-association of ~ (LA) 707
Tungsten, Crystal face dependence of the surface chemistry of ~ (LA) 177
Tungsten complexes, π-Complexes of λ^5-phosphorins with tricarbonylchromium, tricarbonylmolybdenum, or tricarbonyltungsten (SC) 503 [G.E. 543]
Tetrakis(trimethylsilylmethyl)bis(μ-trimethylsilylmethylidyne)ditungsten (SC) 609 [G.E. 692]
Carbonyl-η-cyclopentadienyl-(4-methylphenylketenyl)bis(trimethylphosphane)-tungsten—A novel, stable transition metal-substituted ketene (SC) 632 [G.E. 649]
3-Dimethylamino-3-phenylallenylidene. A novel ligand at the pentacarbonylchromium and -tungsten skeleton (SC) 623 [G.E. 683]
trans-Bromo(tetracarbonyl)ferrocenylcarbyne-tungsten (SC) 683 [G.E. 719]
The photochemical addition of acetylene to tricarbonyl(η^5-cyclopentadienyl)methylmolybdenum and -tungsten (SC) 759 [G.E. 800]
Tungsten compounds, $[W_3O_4F_9]^{5-}$: A complex ion of tungsten(IV) containing a W_3 group (SC) 118 [G.E. 92]
Pentacarbonylmonosulfanetungsten, $W(CO)_5SH_2$ (SC) 366 [G.E. 375]
Dimeric bistetrathiotungstatostannate—A novel coordination compound with nonequivalent and tridentate WS_4^{2-} ligands (SC) 633 [G.E. 691]
Functional transition-metal phosphanes (SC) 769 [G.E. 809]

ULLMANN's Encyclopedia of Industrial Chemistry, Ullmanns Encyklopädie der technischen Chemie (Book Review) 448

VANADIUM compounds, Structure of the "True" metavanadate ion (SC) 374 [G.E. 385]
Vaska complexes, $[Ir\{2,4,6\text{-}C_6H_2(CH_3)_3\}(CO)(PPh_3)_2]$—The first example of cis-trans-isomerism in complexes of the Vaska type (SC) 110 [G.E. 127]
Vicilin, The legume storage proteins legumin and ~ (LA) 318
Vinamidines and vinamidinium salts—examples of stabilized push-pull alkenes (FP) 459 [G.E. 496]
Vinamidinium salts, Vinamidines and ~—examples of stabilized push-pull alkenes (FP) 459 [G.E. 496]
Vinyl compounds, The solvolysis of α-arylvinyl derivatives (LA) 785
Vinylidenedicyclopropanes, Coupling reactions of ~ doubly halogenated in allylic positions—a productive synthesis of trispiro[2.0.2.0.2.0.]nonane ([3]rotane) (SC) 762 [G.E. 803]
Vinyloxiranes, The magnesium derivative of thioacrolein dianion. A facile entry to ~ and divinyloxiranes (SC) 437 [G.E. 449]
Virus diseases, Chemotherapy of ~ (FP) 410 [G.E. 458]
Vitamin B_2, 5-Deaza- and 5-thiariboflavins:

a simple pathway to antimetabolites of ~ (SC) 443 [G.E. 475]
Vitamin B_{12}, New developments in the field of ~: Reactions of the cobalt atom in corrins and in ~ model compounds (FP) 417 [G.E. 465]
Photochemical induction of enzymatic activity of a carbocyclic analog of coenzyme B_{12}: a contribution to the elucidation of the mechanism of action of coenzyme B_{12} (SC) 170 [G.E. 186]
Vitamin B_{12} coenzyme (LA) 563

WAGNER-Meerwein rearrangement, Enantioselective ~ in chiral solvents under high pressure (SC) 243 [G.E. 230]
Wastewater purification, Eutrophication and ~ (FP) 354 [G.E. 354]
Water, Eutrophication and waste-~ purification (FP) 354 [G.E. 354]
Water analysis, Analysis of water (Book Review) 319

XENOBIOTICS, Metabolism of ~ in the lung (LA) 446
Xenon oxide difluoride, $XeOF_2$ (SC) 158 [G.E. 190]
X-Ray diffraction, Röntgenbeugung an Kristallen (Book Review) 565

YLIDES, Cumulated ~ as building blocks for the synthesis of heterocycles (SC) 115 [G.E. 92]
Structure of a phosphorus-nitrogen ylide having twofold coordinated phosphorus (SC) 687 [G.E. 723]
Ynamines, (3-siloxy-3-buten-1-ynyl)amines (SC) 51 [G.E. 59]

ZEOLITE A, Structural chemistry within ~ (LA) 564
Ziegler catalysts, Halogen-free soluble ~ for the polymerization of ethylene. Control of molecular weight by choice of temperature (SC) 630 [G.E. 689]
Zirconium compounds, Hydrozirconation: A new transition metal reagent for organic synthesis (FP) 333 [G.E. 402]
Extreme bond angle distortion in organo-~ active toward ethylene (SC) 629 [G.E. 688]
Zirconium phosphate, Intercalation compounds of ~ (SC) 544 [G.E. 608]